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INDICATIONS FOR THERAPEUTIC ABORTION FROM THE POINT OF VIEW OF THE SURGEON

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The instances in which the surgeon who does not practice in the field of gynecology has to consider the indications for therapeutic abortion or other interference with the anatomic and physiologic components of pregnancy are few. So much is this the case that no one person is likely to accumulate an experience and knowledge in this subject at all comparable to that of the obstetrician and gynecologist. Nevertheless, the surgeon may at any time find himself in a situation where the well-being of the pregnant mother or the fetus or both are imperiled and a crucial decision must be made.

This may be the case with certain surgical diseases which are urgent or of an emergency nature and require immediate operative intervention in order that both mother and child not succumb, even though this may entail some risk of an abortion. Examples of these are intestinal obstruction, perforation of the intestine, acute appendicitis and massive hemorrhage. Other diseases for which the ultimate therapy is operative, but in which the danger is neither immediate nor great, may be handled conservatively until normal delivery occurs, or at least until a viable fetus can be obtained. In instances of these, as hernia of the abdominal wall or hemorrhoids or varicose veins, the mother may suffer discomfort but no damage from delay. Only rarely and under indications not purely surgical would a therapeutic abortion be advisable in these various situations.

Certain common chronic diseases amenable to surgical therapy may cause some minds to weigh the question of therapeutic abortion, only to dismiss it on serious consideration. As an example, the coincidence of thyrotoxicosis and pregnancy is not unusual and is best treated as it would be were it not complicated by pregnancy, or rather as it would have been before the introduction of thiourea and thiouracil. This last reservation is made until further study has determined the effect, if any, of these drugs on the fetus. In any case, to introduce abortion in a patient with hyperthyroidism would be asking for trouble, and were it necessary for other reasons the toxicity should be obviated by medical or surgical means as indicated in the particular patient, before it is attempted.

Another even larger group of diseases is that of malignant new growths and, of particular pertinence to this discussion, the carcinomas in the female. Those associated with the female organs specifically concerned with reproduction, namely the genitalia and the breasts, comprise approximately one half of the morbidity and mortality in the female of what is commonly known as "cancer," the frequency being divided between the two with a small predominance in the breast. It is with the latter that the surgeon is concerned in this discussion, and particularly when carcinomas of the breast are concurrent with pregnancy or lactation.

Fortunately, this association is relatively rare and for several reasons. Only approximately one third of these tumors of the breast occur during the age when nearly all pregnancies take place, namely from puberty to 45; a second third from 45 to 55 is associated with the menopausal changes, and the last third with the involution that goes on with aging.[1] Of the 4,628 patients operated on for carcinoma of the breast and reported by Stewart W. Harrington,[2] there should have been about 1,500 instances in the child-bearing age when the association with pregnancy might be expected to be frequent. The number and distribution of pregnancies in this group was not known, but there were 92 instances of carcinoma of the breast associated with pregnancy or lactation, or about 2 per cent of all the operations, or approximately 6 per cent of those that may be expected to have been below 45 years of age, in all probability indicating a relatively lower incidence of this lesion in pregnancy and lactation than in those women not carrying a child. This agrees of course with the well established understanding that carcinoma of the breast is more frequent in the nulliparous. However, as Grantley Taylor has shown, while the incidence is not increased in young women, the degree of malignancy is, as indicated by the fact that metastases occur earlier and to a greater degree and that therefore postoperative recurrences take place more promptly. This same situation is exaggerated in the pregnant woman as indicated by Harrington's data,[2] according to which in 88 instances of radical mastectomy for carcinoma during pregnancy or lactation 85 per cent had spread beyond the breast and only 15 per cent not. The survival rates in those having axillary metastases were, at three years, 17.3 per cent and at 5 years 5.5 per cent, while for those with the growth confined to the breast the rates were 65.5 per cent at both three

Read in a Panel Discussion on Modern Indications for Therapeutic Abortion before the Section on Obstetrics and Gynecology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 11, 1947.

1. Nathanson, I. T.: The Relationship of Hormones to Diseases of the Breast, Surgery 16: 108-140, 1944.

2. Harrington, S. W.: Carcinoma of the Breast: Results of Surgical Treatment When the Carcinoma Occurred in the Course of Pregnancy or Lactation and When Pregnancy Occurred Subsequent to Operation (1910-1933), Ann. Surg. 106: 690-700, 1937.

and five years. Whatever significance this may or may not have as regards therapeutic abortion, it does indicate that the obstetrician and surgeon during pregnancy should examine the breasts frequently and carefully in the hope of detecting a tumor early, when it may be still confined to the breast. If it proves to be malignant, then a radical mastectomy must be done.

Only when these data are at hand should a decision be made as to an abortion. It is clear, as Grantley Taylor [3] has pointed out, in young women that once the malignant lesion is established, therapy of any nature will not change its biologic characteristics, and I think one may include in this the removal of the fetus and placenta. Certainly when there is a spread beyond the "breast" it would be illogical to destroy one life in order to attempt to retrieve a nearly hopeless situation in the parent, particularly in view of the fact that there is no evidence that doing this would in any way change the course of the disease. When the growth has not extended beyond the breast, probably indicative of its relatively lower malignancy, and when the outlook is much more favorable, there is still less reason to terminate the pregnancy, and particularly if it is beyond the third month. There may be adequate reasons for doing so previous to this time, other than malignant disease, but these do not fall within the province of the surgeon.

As regards nursing the baby, it is largely an academic question, for with one breast removed it is unlikely in these days that the remaining breast will be so employed. In fact, it is not certain that it is either beneficial or dangerous. In any case, during pregnancy and lactation it is necessary to follow closely the residual breast, for under these conditions the frequency of involvement is probably somewhat increased.

As regards pregnancy following a radical mastectomy for carcinoma not occurring in conjunction with pregnancy, Harrington's [2] experience is of interest. There were 55 such instances, of which he was able to follow 37. Of these patients 33 lived one or more years after the birth of the baby, and, of the 12 patients who had live babies fifteen or more years previously, 7 were living. He advised those having had carcinoma of the breast not to go through further pregnancies, and if they had children not to nurse them. In fact, there is not sufficient factual information to be certain that this advice is necessary. On the other hand, it might be well for the patient to avoid pregnancy for three or four years subsequent to a radical resection, in order to obviate the possible simultaneous occurrence of a pregnancy and a recurrence. So far this discussion because of its bearing on therapeutic abortion has been governed by the "curability" of established carcinoma of the breast, which involves, so far as is known at the present time, the detection and destruction of the primary focus before spread has occurred. Once this is accomplished, further measures are unnecessary, but if the disease is elsewhere, then the treatment is palliative, in the hope of slowing up its progress and of ameliorating the distressing symptoms. While a "cure" should always be striven for and is an end devoutly to be desired, at the present time in the majority of instances of carcinoma of the breast it still remains true that the therapy is palliative.

For many years it had been suspected that changes of the breast were dependent on ovarian function. With the discovery and intensive study of the estrogens and of their effect on the development of the breast in the experimental animal, particularly the production of "cancer of the breast" in the male mouse of a tumor-susceptible strain, the hope of effecting a cure or of producing palliation by the cutting off of estrogens, or by their "neutralization" with the androgens, has come to the fore. That the former can be accomplished seems extremely unlikely in view of present knowledge, for, as Nathanson [1] said, "the estrogens in themselves are not carcinogenic, but merely provide the substrate upon which an exciting agent may act." Furthermore, while they may have a great deal to do with the initial change from benignity to malignancy, once the growth becomes autonomous and is capable of growing on heterologous transplantation in either male or female animals, it is obvious that changes in either estrogen or androgen are unlikely to destroy it. Nevertheless, the ablation of the testicles or the administration of estrogens in carcinoma of the prostate as initiated by Huggins has demonstrated in many instances at least definite palliation.

Consequently, at the present time there is a recurrent interest in the "sterilization" of the female with carcinoma of the breast, by radiation of the ovaries or by their ablation when cessation of menses has not occurred. As long ago as 1905 Hugh Lett [4] in England reported 99 instances of "incurable carcinoma of the breast in which bilateral oophorectomy was done, with marked improvement in 22 and distinct improvement in an additional 35." These beneficial results he described as "relief of pain, improvement in health, diminution or disappearance of growth, healing of ulcers and prolongation of life." He was probably over-optimistic in his interpretation, and others who followed his lead did not obtain so good results or became discouraged at palliation, which in the end arrived at the same ultimate result.[5] Similar findings are now being obtained in perhaps a third of those patients who are suffering from pain due to metastases to bone. In addition to the cutting down of the production of estrogen in this manner, which is by no means complete, the use of testosterone [6] is being tried out, with apparent beneficial results in some instances.

These attempts at hormonal therapy are as yet experimental and directed at palliation of existing disease. There is no indication at the moment that they will effect "cures" or prevent cancer, and, indeed, in careless hands it is possible that they may do more damage than good. It would be better to leave their use to those having adequate clinical material, sufficient knowledge of these hormones and critical judgment, until the proper indications and methods of application are fully developed.

3. Taylor, G. W.: Carcinoma of the Breast in Young Women, New England J. Med. 215:1276-1278, 1936.

4. Lett, H.: An Analysis of Ninety-Nine Cases of Inoperable Carcinoma of the Breast Treated by Oophorectomy, Lancet 1:227-228, 1905.

5. Taylor, G. W.: Evaluation of Ovarian Sterilization for Breast Cancer, Surg., Gynec. & Obst. 68:452-456, 1939.

6. Adair, F. E., and Herrmann, J. B.: The Use of Testosterone Propionate in the Treatment of Advanced Carcinoma of the Breast, Ann. Surg. 123:1029-1035, 1946.

Thoracolumbar Sympathectomy.—The surgical treatment of hypertension had its origin in the pioneer work of Crile, Adson and Craig, Page and Heuer, Peet and others, but it was not until 1940 when Smithwick first reported his clinical studies that an efficient operative procedure was made known.—Hinton, J. W.: *Bulletin of the New York Academy of Medicine*, April 1948.

THERAPEUTIC ABORTION FROM THE POINT OF VIEW OF THE INTERNIST

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From the point of view of the internist, diseases of the cardiovascular system far outweigh any other possible indications for therapeutic abortion. This is a corollary of the fact that pregnancy tends to increase both cardiac output and blood volume. As Burwell[1] has observed, pregnancy produces cardiodynamic changes similar to those which characterize arteriovenous fistula. Within certain limits, these changes are reversible in both instances.

Let us first consider hypertension which grows steadily worse as pregnancy proceeds. This includes hypertension which existed prior to conception, as well as that which appears during gestation. Certain observations[2] have indicated that many women with hypertension, even when they have albuminuria, edema or headache, bear children without immediately discernible ill effects to themselves or their offspring. In such cases, however, the probabilities are that the hypertension is fundamentally benign and that it will abate to a considerable extent after delivery. It is another matter when the diastolic pressure manifests an ever increasing upward tendency, especially during the first trimester. Hypertension of this variety, with a diastolic level rising above 110 mm. of mercury, must be considered actually or potentially malignant, and therefore should constitute an indication for abortion. This indication becomes imperative as soon as impairment of the function of either the heart or the kidneys can be demonstrated.

It is well known that women with old cardiac valvular lesions, including mitral stenosis, often bear one or more children uneventfully. In these cases the lesion must be minimal from the dynamic point of view, or the patient must have lived such an elaborately sheltered life that having a baby was the only real work she ever did. In deciding which patients with valvular heart disease should be allowed to go to term, one must consider the age of the patient, how much cardiac hypertrophy she has, evidence of congestive heart failure, past or present, and the mechanism of the heartbeat.

Age need not be discussed, for it is obvious that, other things being equal, the younger the patient, the better her chances.

The amount of cardiac hypertrophy is particularly important. Generally speaking, hypertrophy develops in direct proportion to (1) the degree of mechanical embarrassment produced by the valvular lesion and (2) the extent to which the myocardium was involved in the original inflammatory process. This generalization, however, is beset with disconcerting exceptions which tax the resourcefulness of the cardiologist. Chief among these is the conjunction of a mechanically severe lesion with minimal hypertrophy. If, in addition, the auscultatory signs are misleading or wanting, the disease is virtually undiagnosable by ordinary clinical methods and recourse must be had to special procedures which cannot be described here.

In all cases in which ventricular hypertrophy is present, the amount of the hypertrophy is much more important than the valvular lesion, regardless of its severity or location. It is impossible to overemphasize the old observation that the greatly hypertrophied heart is a severely damaged, and therefore a seriously weakened, heart. Cardiac hypertrophy not only encroaches directly on the myocardial reserve, but also greatly diminishes the efficiency of the heart by increasing the amount of cardiac residual blood. This increase may amount to as much as 1,000 to 1,200 cc., which means, of course, that each systole can do no more than skim the surface of the pool.

The pathologist quickly ascertains the degree of cardiac hypertrophy by weighing the heart, but the clinician must rely on indirect methods. If, in the absence of congestive failure, the heart is demonstrably enlarged, hypertrophy is presumably present, but this is strictly inferential, and, if the hypertrophy is more concentric than eccentric, its extent will always be underestimated. Furthermore, simple hypertrophy alone probably constitutes less of a hazard to the patient than hypertrophy plus an increase in cardiac residual blood. Therefore, in order to improve the clinical estimate of the degree and kind of hypertrophy and to ascertain as accurately as possible the amount of cardiac residual blood, careful measurements of the arm to tongue circulation time must be made. Discounting the changes in circulation time caused by pregnancy itself, the greater the prolongation, the larger the risk.

Congestive heart failure which tends to progress in spite of treatment and is characterized by an increase in systemic or pulmonary venous pressure, or both, constitutes a clearcut indication for therapeutic abortion, regardless of whether the failure antedated the pregnancy. If the patient has had congestive failure in the past, as attested by the history, permanent cardiac enlargement and enlargement of the liver, without hepatic pain or tenderness, pregnancy may be allowed to proceed only if extraordinary precautions are taken and the patient is kept under close observation. Some patients with a chronic, nonprogressive form of heart failure, in which there is no increase in venous pressure and moderate edema is the principal manifestation, often tolerate pregnancy surprisingly well.

Some of the disturbances in the mechanism of the heartbeat are dynamically or symptomatically so serious and so intractable that they may constitute an indication for therapeutic abortion. Included among these are acquired auriculoventricular heart block and bundle branch block, and chronic and paroxysmal auricular fibrillation, auricular flutter and ectopic tachycardia, particularly ventricular tachycardia. If the patient also has chronic valvular heart disease, the indication often becomes urgent. Congenital auriculoventricular heart block or bundle branch block, if unaccompanied by other lesions, introduces no maternal risk whatsoever.

If acute rheumatic heart disease or subacute bacterial endocarditis develops during pregnancy, the indication for abortion is imperative and immediate, despite the fact that, in the case of the latter, modern chemotherapeutic methods often effect a cure. Fortunately, the incidence of these diseases during pregnancy is extremely low

Before leaving the subject of cardiovascular disease as an indication for therapeutic abortion a few ghosts which seem to survive only in textbooks of obstetrics

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1. Burwell, C. S.: The Placenta as a Modified Arteriovenous Fistula Considered in Relation to the Circulatory Adjustments of Pregnancy, Am. J. M. Sc. 190:1, 1935.

2. Sharley, J. A., and Hess, C. B.: The Effect of Essential Hypertension on Pregnancy, Am. J. Obst. & Gynec. 50:672, 1945.

137
948

should be laid. There is nothing to substantiate the assertion that the maternal heart undergoes hypertrophy as a result of pregnancy, as any internist who has examined many mothers of many children knows well. Dilatation of the right ventricle occurs under certain circumstances, but it has nothing specifically to do with pregnancy. A pulsation in the veins of the neck is normal when the patient is recumbent. If it occurs in the sitting position, it indicates an increase in systemic venous pressure, which is one of the signs of congestive heart failure. This subject has already been discussed. Geographic location is unrelated to the incidence of rheumatic heart disease, as Army and Navy reports have shown. It has often been said that many pregnant women have "functional" heart murmurs. If a murmur did not function, it could not be heard, and therefore all murmurs are "functional," but some which appear to be endocardial are extracardial. Making the distinction is a problem for the student of physical diagnosis, not for the accoucheur. Finally, digitalis is not indicated in all cases of heart disease or heart failure and must not be prescribed indiscriminately.

In cases of pulmonary tuberculosis, pernicious anemia and diabetes mellitus, abortion may occasionally be indicated, but not as a rule, for the treatment of these diseases is now so successful that pregnancy may safely be allowed to proceed to term. Severe hepatitis or ulcerative colitis may make abortion advisable, but diseases such as leukemia, lymphoma and polyneuritis obviously do not.

PANEL DISCUSSION ON MODERN INDICATIONS FOR THERAPEUTIC ABORTION

S. A. Cosgrove, M. D., N. J., Moderator

Dr. Catherine MacFarlane, Philadelphia: I was much interested in Dr. Harvey's discussion of the need for therapeutic abortion in women with cancer, particularly with cancer of the breast. I was reminded of Dr. Bittner's demonstration some years ago of the milk factor as an agent in the transmission of cancer in strains of susceptible mice. Applying this to women, it would seem that complete elimination of nursing with cancer of the breast or other organs would be indicated. Perhaps this procedure would eliminate the necessity for considering the production of abortion in these women who happen to be pregnant and also have cancer of the breast.

Dr. Marie Pichel Warner, New York: The woman physician is besieged with more requests for abortion for real or imagined therapeutic indications than the male physician. There are many cases in which the indications for therapeutic abortion are not clearly defined. What, for example, should be one's attitude in advising a patient who requests a therapeutic abortion because she had suffered from a depressive state for which she had been institutionalized and had been treated with shock therapy? A normal woman has a strong maternal drive. Is it not possible, then, that the very fact that a woman appeals to a physician for therapeutic abortion is an indication of sufficient mental and emotional imbalance to warrant a therapeutic abortion followed by psychotherapy? The mental reaction and future of the unmarried pregnant woman in terms of personal shame and disgrace to the family, when she is forced to have a child which she places for adoption, should be the subject of serious consideration as a psychiatric indication for therapeutic abortion. There is at present no satisfactory solution to this problem. There is also the problem of the woman of menopausal age who becomes pregnant. She may not have a serious organic indication for therapeutic abortion, but psychologically develops a severe anxiety state about her middle age. When strong fears exist regarding the outcome and delivery at middle age, and her feeling of inability to handle an infant and a belief that her age restricts a normal parent-child relationship, what should be advised? The saddest cases are those of married women who are not yet ready to have babies for economic or other reasons. They have an illegal abortion and then soon after, because of the psychologic reactions, are driven to desire a pregnancy and find that they have become sterile after the recent abortion. One tends to think of the child in all these cases, but still one owes something to the woman. At least, one should try to help her constructively and not just evade the question by saying, "I'm sorry, I can't help you. Go elsewhere. You have to do the best you can. Abortion is illegal." All of these replies are not helpful. I should like more constructive advice and help with the problem of handling the case of the single girl who is in the early months of her pregnancy. The prevention of illegal abortion with its concomitant maternal morbidity and mortality can be helped best by broadening and liberalizing the interpretations of medical indications to include the social and mental hygiene problems of each particular case. Sex education, a biologic understanding of conception and premarital marriage information are preventives for unplanned pregnancies, which eliminate the question of abortion, both therapeutic and illegal.

DEPRESSIVE STATE

Dr. E. W. Busse, Denver: Dr. Warner's questions concern problems which physicians frequently encounter and on which they are asked to make decisions. The first case which Dr. Warner cited was of a young girl who had a depression, was given electric shock therapy, is now illegitimately pregnant and wants an abortion. This is a case which rests on the careful evaluation of the patient by the psychiatrist for the simple reason that he first must decide how severe this depression is or was. For instance, at the institution with which I am associated we do not ordinarily believe in giving electric shock therapy to patients with psychoneurotic depressions. Some psychiatrists do. If it were merely a neurotic depression, I would not recommend a therapeutic abortion. However, if the depression was a recurrence and was rather severe, and if the pregnancy allowed to go to term would prevent her eventual recovery, I would recommend a therapeutic abortion.

THE ECONOMIC FACTOR

The second problem presented involves a woman who comes in wanting an abortion, stating that she is not economically ready to have a child. This is not a question for the physician to decide, whether a person is economically able or not. An abortion is certainly not justified. Some persons want a lot more financial security than do others before starting a family. A psychiatric problem is frequently present when a person asks for an abortion and gives as an excuse poor economic conditions. I believe it is best to talk not only to the potential mother but also to the husband and to find out where he fits into the picture. It is often the husband who is at fault, insisting on an abortion. He may be a poorly adjusted person, and if he can be helped a difficult marital situation may be improved.

INCEST

Question: What would be your attitude and the attitude of your committee in a case of incest?

Question: One of my patients had a daughter who was impregnated by the father.

Dr. Busse: I would probably recommend a therapeutic abortion. It has been my experience that a girl who is in such a situation, where the father will force her into sexual activities, is in an extremely poor home environment. That child is often a candidate either for a psychosis or for a life of antisocial behavior. Final opinion, of course, would rest on the child's mental condition, but often a therapeutic abortion is justified. The patient should have the benefit of psychiatric care, to do something about her future and to prevent a major mental illness.

RAPE

Question: Would that situation apply also to rape?

Dr. Busse: I believe that the justification of therapeutic abortion depends on the patient's mental condition and her attitude regarding her unwanted pregnancy.

MENOPAUSE

Question: What about the woman in menopause? Don't you think that the woman is afraid not because she is pregnant but because of the fact that the neighbors will talk about her since she is 43 or 45 years old and is pregnant? Don't you think that by means of radio, education, newspapers, etc., a woman could be helped to hold the baby?

DR. BUSSE: The point has been raised that if a woman is going through the menopause, or is near it, and becomes pregnant she frequently worries about how the neighbors will feel and wonders what to do about it. Certainly proper education by any means is desirable. I certainly would not, off hand, recommend a therapeutic abortion unless the patient is faced with a psychotic break from which she might never recover. Otherwise, I do not believe that I would be justified in doing anything, especially if she has been a perfectly well integrated person up to that time.

GERMAN MEASLES

THE MODERATOR: A number of inquirers are specifically interested in the recently much discussed necessity for therapeutic abortion in mothers who have had German measles in the early part of their pregnancy.

MEMBER: I think there is a bit of confusion. It is chickenpox, not German measles.

THE MODERATOR: German measles; several have inquired about that. I myself cannot answer that question. I feel that we have too quickly gone overboard on the inadequate evidence that has been accumulated thus far as to what proportion of women suffering from German measles early in pregnancy are going to have defective offspring. Until that question is answered by a greater accumulation of experience, I am afraid that none of us can answer the question as to the necessity of abortion for every woman who has German measles during the early part of her pregnancy. That is an inadequate answer, but it is the only answer that I feel competent to make at this time.

VACCINATION

QUESTION: Recently in New York city, in connection with the epidemic of smallpox, the Health Department was asking whether women in early pregnancy should be vaccinated. The Health Department decided not to vaccinate during early pregnancy for fear that these women might possibly have defective children.

THE MODERATOR: There has recently been in the New York metropolitan area not an epidemic but several sporadic cases of smallpox which have been fatal. The Health Department of the city and state thereupon properly seized upon that circumstance in an effort almost to coerce the population into widespread vaccination. Every pregnant woman within 50 miles of New York City Hall wanted to know about the advisability of vaccination. Inasmuch as German measles is a virus disease, many physicians thought that if a woman is inoculated with another active virus the effect on her offspring might be similar to that which is supposed to result from German measles. Many physicians, including myself, advised their pregnant patients to have it done. The Health Department did not have the courage to make it obligatory on such women. I think that within the next two or three years the results will be available of what constitutes a great mass experimentation in regard to this matter which no one has heretofore had opportunity to observe. We should all anticipate the conclusions to be drawn from the observations of that great mass experiment.

BUERGER'S DISEASE

QUESTION: Should abortion be induced in a woman with Buerger's disease?

DR. H. M. KORNS, Dubuque, Iowa: Buerger's disease is extremely rare in women, but, if this question should arise, it could not be answered without careful study of the entire cardiovascular system, for Buerger's disease often involves visceral, as well as peripheral, arteries and veins.

THERAPEUTIC ABORTION CAUSE OF STERILITY

MODERATOR: What about the woman who has procured a therapeutic abortion, the indication for which is not specified, who thereafter is unable to conceive and becomes desirous of having a child? I think that Dr. Busse touched on that in his original discussion. Do you want to elaborate on it, Dr. Busse?

DR. BUSSE: I will go over that question as I understand it. I may be wrong. The woman had a therapeutic abortion and thereafter wanted a child but was unable to conceive. What is going to happen? Such a woman may develop guilt feelings and become depressed and suicidal. These patients are difficult to handle. Frequently the psychiatrist has no way of treating them other than use of electric shock therapy. After the depression has begun to improve, then it often becomes a matter of prolonged psychotherapy. In the cases of less severe depression it is sometimes possible that the patient will eventually become capable of accepting an adopted child as a substitute. However, that is an individual problem, and I am afraid that I cannot generalize because each patient must be separately evaluated.

THE MODERATOR: I think that all the essayists have sufficiently developed the important point that every case in which therapeutic abortion is proposed must be carefully individualized. Some of the questions cannot be answered categorically, inasmuch as individual considerations would vary greatly.

HYPERTHYROIDISM

QUESTION: A patient a year ago had a thyroidectomy for hyperthyroidism. She quieted down and had a perfectly normal basal metabolic rate after the thyroidectomy. Within a year she became pregnant. After she became pregnant there was a recrudescence of her hyperthyroidism with a high basal metabolic rate comparable to that which she had prior to the operation.

DR. S. C. HARVEY, New Haven, Conn.: It is not unusual to have hyperthyroidism in conjunction with pregnancy. My reaction to it would be exactly as I have said previously, that that patient should be treated as if she were not pregnant, by medical means. If you induce an abortion, you are likely to precipitate the thyroid storm and have much more difficulty with the thyroid situation as a result of the abortion.

TUBERCULOSIS OF BLADDER

QUESTION: A patient whose ureters have been transplanted because of tuberculosis of the bladder is now four months pregnant, and has an attack of pyelitis. Should abortion be induced? She has no children and would like to have one.

DR. HARVEY: That is distinctly a situation that has to be decided with all the factors in hand. Certainly a person who has so severe tuberculosis of the bladder as to require transplantation in all probability has tuberculosis of the kidneys, also. The pregnancy would be a rather dangerous business. On the other hand, if she wishes to take the risk and insists on it, that, after all, is her own decision.

THE MODERATOR: Emphasizing what Dr. Harvey has said, although in this situation even the urologist would not apply urethral drainage in the same way as he would in a normal woman, there is still enough resource in the use of antibiotics and other modern drugs to keep her pyelitis under control, so that it would seem to me worth while at least to attempt to save for her this baby.

TOXEMIA

QUESTION: A patient is 41 years old. She had had her first pregnancy at 33. She had toxemia at the seventh month in that pregnancy, characterized by porphyrinuria, hypertension and edema. She was allowed to go to term and delivered a healthy baby. In her second pregnancy at age 38 she had toxemia with similar symptoms but beginning earlier, this time in the fifth month. She was carried through that pregnancy also by four months of continuous bed rest, survived the pregnancy and was in good health. Her baby lived. Now, at 41, when she is only two months pregnant, she again shows toxemia characterized by headache and a blood pressure of 160 systolic and 110 diastolic. What should be done in this case?

DR. KORNS: I think that the obstetrician could help answer that question. I would have to examine the patient and form an estimate of her myocardial reserve. I have seen such patients, however, who I thought could continue with the pregnancy safely if they were closely watched.

THE MODERATOR: I am glad to see that Dr. Korns, assuming that this woman did not have any pronounced cardiac impairment or impairment of renal function, would be moderately encouraged to attempt to carry this woman through her pregnancy, even though the toxemia has appeared so early. That refers to some of the things which he said in his paper about hypertension per se. I certainly concur with him and would be glad to attempt to carry this patient through to a third successful termination.

Rh Incompatibility

Question: A patient has lost 2 infants—presumably because of Rh incompatibility between husband and wife. What is the prognosis in this situation?

Dr. Hudnall H. Ware Jr., Richmond, Va.: We had had the experience of seeing a patient who lost her first baby, apparently from an Rh incompatibility. The second baby was born alive and lived. The third baby again was lost through an Rh incompatibility. The patient's husband was Rh positive and heterozygous as determined at the third pregnancy, and the wife was Rh negative. In the fourth pregnancy a rather severe toxemia developed at the seventh month with edema and elevation of the blood pressure, but no urinary changes. She was put to bed and her condition improved. She was carried to term and delivered of a living baby this time. In commenting on the case which Dr. Cosgrove has referred to me, I recognize that Dr. Levine and Dr. Diamond, both authorities on this subject, do recommend for abortions certain selected patients who have had proved Rh incompatibilities. Studies to determine whether the husband is heterozygous or homozygous would be helpful. I would try to carry this patient to term if her condition remained good, hoping that she might be one of the lucky ones. I would have her blood examined regularly and watch for an increase in the antibody titer. I would consult one of the experts on Rh studies for advice in treating the patient.

Multiple Sclerosis

Question: Should abortion be induced in the patient with multiple sclerosis? She is now in the midst of a four year remission, is 32 years old and is apparently in good health.

Dr. Busse: In my brief experience, patients with multiple sclerosis are apt to have an exacerbation during pregnancy. I would base my decision on the severity of the condition and the period of time which has elapsed since the last exacerbation. If the patient's symptoms are mild and she is anxious to have the child, I can see no reason for terminating the pregnancy. If she is rather ill and it is probable that the pregnancy will make her condition worse, I would recommend a therapeutic abortion.

The Moderator: A colleague in a nearby city has just successfully brought such a patient through her pregnancy who had no relapse during pregnancy and no sign of deterioration, after the faculty in the local medical college had refused to take the responsibility of carrying her through. Again there is the need for individualization and care in acting too much on strictly didactic principles.

Tuberculosis in Husband

Question: A man, bedridden with tuberculosis, gets his wife pregnant. She is the only one to take care of him. Should an abortion be induced?

The Moderator: No; as an obstetrician I refuse to be the habitual mechanician of fools who are too selfish and ignorant to take care of themselves.

Spotting

Question: How does the panel feel concerning the interruption of pregnancy because of frequent spotting during the first trimester? Many subscribe to the theory that the bleeding may be a natural effort to rid the patient of pregnancy with defective germ plasm and subsequent defects are proved by the condition of the baby.

Question: Let's go a little further and say these patients have had two successive pregnancies, with malformation of the fetuses, hairlip or hydroencephalus. We have had four requests in the past year for therapeutic abortion for such patients. Let's go further and ask whether a patient has had two successive malformations—not one, because it is known sometimes that the next will be a perfectly normal baby, but two—should we consider a therapeutic abortion at their request because they do not want to go through with the third pregnancy?

The Moderator: I do not think so. I have seen such patients repeatedly have perfectly normal babies. One never knows what kind of baby he is destroying when he does an abortion. It may be the best baby that patient has ever had. He has no means of knowing.

My answer to that would be categorically no.

Cesarean Sections

Question: How many cesarean sections should be allowed before a therapeutic abortion should be done?

The Moderator: Well, what a foolish thing it is to do a therapeutic abortion just because a woman has had two or six or ten previous cesarean sections. Let her go ahead and have this further one by section. Sterilize her then, if you like.

Summary by the Moderator

There is a phase of this situation that none of the discussers touched on, which is important. Both Dr. Korns and Dr. Harvey have indicated that in spite of the number of situations in which they recognize the necessity for therapeutic abortion, women with all kinds of impairments, in their experience, can be carried safely through pregnancy, no matter what the precise nature or degree of severity of the symptoms which may present themselves, if one can give them extremely careful medical and surgical attention. Medical and surgical treatment costs money. The vast majority of these patients who could afford the costs of an ordinary parturition cannot afford the cost of four to six months' hospitalization. They do not all live in great metropolitan centers where the public hospitals can subsidize that cost through facilities already provided out of tax funds. Eleemosynary sources are not available or are inadequate to do it. And yet, if medicine is going to do its job, if it is going to conserve human life unborn with just as much assiduity and conscience as it devotes to conserving adult human life, a means must be found to subsidize the patient with rheumatic heart that has to be kept in bed, for instance, all during pregnancy. We have a broad problem attending this matter of the conservation of fetal life; that is, the provision of subsidy from public funds at some level—municipal, state or federal—for persons suffering from numerous complications of pregnancy, in the same sense that the campaigns against tuberculosis, syphilis, poliomyelitis and cancer are being subsidized by governmental funds in addition to great voluntary popular subscription. Rheumatism and rheumatic heart disease particularly are next on the list of the great scourges of mankind that will have to be so subsidized. Call that state medicine, if you will; I do not care; I have long since learned not to shy too much at the bugaboo of state medicine, because we have state medicine with us in a large degree and have had for half a century. But if we are going to answer this whole question satisfactorily, the sufferers from many of these diseases must be helped, and the only source of help that I can envisage as available to them on a large scale is public money. It is the duty of this Association to give serious thought to the means of seeing that that great want is supplied. I should like to summarize in a personal fashion, without any reflection on the opinions of these fine men who have provided us with so much worth while thoughtful material this morning. The medical profession from the nature of its work and obligation is and must continue to be a highly ethical group. A high sense of this ethical obligation must be thoroughly instilled in members of the medical profession during their undergraduate experience. The responsibility for this ethical training resides in medical teaching faculties. This responsibility entails organized, positive efforts toward its fulfilment. Nowhere does this ethical sense have more direct bearing than in relation to abortion. Widespread and indiscriminate abortion is a major factor in puerperal mortality. It is believed to be best controlled by retention of the ethical recognition that the fetus is a human being with all the potentialities of every human being; that its destruction is murder, only justifiable in the most extreme circumstances involving direct and imminent threat to the mother's life; that corollary improvement in the whole situation must depend on the wide development of one of the four freedoms given as the goal of our national development, that of freedom from want, and that in the preservation of the ethical sanctity of fetal life and the development of this freedom in all its phases lies more hope of eventual betterment of the general abortion abuse situation than a reversion to the amoral and unethical plane of the most primitive and debased societies. It is the duty of medical bodies to formulate and supply a specific code for the ethical guidance of the members of our profession in relation to this problem.

HEALTH SERVICES FOR THE RURAL CHILD

Availability of Hospitals, Physicians and Dentists in Service Areas

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The "National Health Program" of the American Medical Association states that "every child should have proper attention, including scientific nutrition, immunization and other services . . ." Those members of the American Medical Association who have special interest in the field of child health and who belong to the American Academy of Pediatrics have, through an official statement of the Academy, endorsed a similar objective of better medical care and health supervision for all children. Not only private medicine but government and farm groups as well are committed at national, state and community levels to an objective of more and better health services for the rural child.

Convinced that physicians, who are caring for children in their daily practice, must assume a greater share of the responsibility for planning for the improvement of child health, the Academy has undertaken an active program to provide better and more evenly distributed health services for all children irrespective of race, economic status or geographic location. As a first step, the Academy set out to learn the facts concerning existing health services for children so that, with a full knowledge of present conditions, well considered opinions and recommendations might be reached.

A nationwide study of child health services was therefore instituted with the cooperation of the United States Public Health Service and the United States Children's Bureau. During the course of this study, which is now nearing completion, an intensive survey has been made of hospitals, private practice of physicians and dentists, community health agencies and the pediatric training given by medical schools. Much of the information has been collected by personal visits to hospitals, health centers and medical schools. Mail questionnaires to physicians and dentists have brought an exceptionally high percentage of response. The study has been both broad in scope and detailed in its investigation. At the national, state and local levels, facts have been gathered with a definite purpose in mind: to provide the tools with which to improve child health, not only for the country as a whole but for every local community. Therefore, certain of our data are being tabulated for each of the 3,076 counties.

SERVICE AREAS BASED ON COUNTY GROUPS

Inequalities are known to exist in health services for the rural child in comparison with those for the urban child. We undertook to determine the extent and nature of these inequalities in specific detail. But at the outset we accepted the fact that the usual differentiation between rural and urban is unsatisfactory for comparisons in medical services. Many persons living in rural areas are at the same time near enough to urban centers to permit easy access to the facilities of those centers. However, in rural areas far removed from urban centers, services received are, for the most part, restricted to those which can be obtained locally.

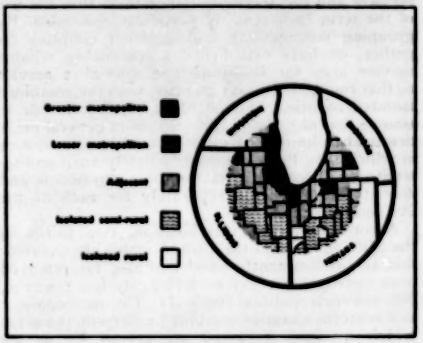

Fig. 1.—Example of county grouping.

Therefore, service areas have been established recognizing two fundamental characteristics: *(a)* population and *(b)* proximity to densely populated areas. In this way, consideration is given to areas which, although they themselves may be sparsely populated, are nonetheless relatively close to metropolitan areas and the medical facilities ordinarily available in such centers.

For practical purposes, service areas have been established so as not to cross county lines. Five groups of counties have been created. Metropolitan counties, which include the metropolitan districts of cities of 50,000 or more persons, have been subdivided into "greater metropolitan" and "lesser metropolitan," the former being in or around the twelve major cities of the United States. Counties geographically contiguous to any of the metropolitan counties are classified as "adjacent." The remaining counties have been subdivided into "isolated semirural" and "isolated rural," depending on the presence or absence of an incorporated place of 2,500 or more inhabitants.[1]

From the American Academy of Pediatrics Study of Child Health Services and the Division of Public Health Methods of the United States Public Health Service.

Read at the third annual meeting of the National Conference on Rural Health of the American Medical Association, Chicago, Feb. 6, 1948.

Because of lack of space this article has been abbreviated in THE JOURNAL by the omission of tables 4 and 5. The complete paper will be found in the authors' reprints, which the authors will be pleased to send on request to the American Academy of Pediatrics Study of Child Health Services, 2346 Massachusetts Ave., N.W., Washington 8, D. C.

1. A county is classified as metropolitan if it has at least one city of 50,000 or more inhabitants. Counties are also classified as metropolitan if they include *(a)* densely populated areas touching metropolitan counties (adjacent and contiguous minor civil divisions which have a population of 150 or more per square mile), and *(b)* 50 per cent or more of the population of the county or at least 50,000 people within such densely populated areas. A greater metropolitan county is one in which there is located any part of metropolitan districts of 1,000,000 or more inhabitants in and around the cities of Baltimore, Boston, Chicago, Cleveland, Detroit, Los Angeles, New York, Philadelphia, Pittsburgh, St. Louis, San Francisco and Washington. Lesser metropolitan counties are all other metropolitan counties. Counties that touch a metropolitan county but are not themselves metropolitan have been classified together as adjacent counties, unless the nearest point of the county is more than 50 road miles (80.5 kilometers) from a city of 50,000 or more population. (A few nearby counties were classified as adjacent, on the basis of travel habits of the people, although these counties did not actually touch a metropolitan county.) Counties that do not touch any part of a metropolitan county have been subdivided into isolated semirural and isolated rural counties. An isolated semirural county has at least one incorporated place of 2,500 or more inhabitants, and an isolated rural county has no incorporated community of 2,500 or more inhabitants.

Figure 1 illustrates the county groups in and around the city of Chicago. The classification of each county in the United States is given in table 6.

The unusual feature of this manner of classification is in the use of the adjacent category.[2] It is recognized that a large hospital in an urban center serves not only the county in which it is located but also the surrounding counties. It is for hospital services and the services of specialists that the use of the term "adjacent" is particularly suitable. By grouping metropolitan and adjacent counties together, we have established a reasonably reliable service area for hospitals and specialist service so that comparisons may be made with the combined isolated counties. On the other hand, it is fair to assume that physicians and dentists in general practice tend to limit their practice to the communities in which they live or the immediately surrounding territory. Therefore, data for these physicians and dentists are discussed separately for each of the five county groups.

According to this classification, two thirds of the 3,076 counties in the United States are isolated; that is, predominantly rural and also far removed from metropolitan centers. Relatively few counties, 240, are metropolitan (table 1). The metropolitan and adjacent counties combined represent the areas which we have assumed are served by or are readily accessible to large urban medical centers.

TABLE 1.—*Counties in the United States by County Group and Size of Largest Urban Place, 1940*

	Total counties	Counties with an Incorporated Place of 50,000 or More Persons	Counties with an Incorporated Place of 2,500 to 50,000	Counties with an Incorporated Place of Less than 2,500
Greater metropolitan	63	34	29	0
Lesser metropolitan	177	130	47	0
Adjacent	668	—	472	196
Isolated semirural	1,116	—	1,116	—
Isolated rural	1,052	—	—	1,052
Total	3,076	164	1,664	1,248

Many of the adjacent counties (almost one third) are in themselves entirely rural by definition of the United States Census; that is, they have no incorporated place of 2,500 persons or more. However, since their inhabitants have the advantages of living near medical centers, they are much more favorably located than persons who live in the counties which are isolated as well as rural.

TABLE 2.—*Rural Population and Density of Population in the United States, by County Group, 1940* *

	Percentage of Total Population That Is Rural	Persons per Square Mile
Greater metropolitan	11	1,136
Lesser metropolitan	24	193
Adjacent	68	42
Isolated semirural	64	26
Isolated rural	100	19
Total	41	41

* From: Sixteenth Census of the United States: United States Department of Commerce, Bureau of the Census, 1. Population, United States summary, table 17, 1940.

Table 2 shows for each county group the proportion of the total population that is rural. In our classification, the only county group which is 100 per cent rural by definition is our isolated rural. About two thirds of the population of the isolated semirural and of the adjacent counties are rural, while even the population of the group of greater metropolitan counties is 11 per cent rural. Expressed in terms of density of population, the contrast is even more striking among the five county groups.

Analysis for individual states shows that there is a high degree of correlation between our county classification and counties grouped according to the size of their largest urban place.[3]

In any study of the availability of medical care, consideration must be given to the economic status of the community and to the individual's ability to pay. We have found a close correlation between our classification of counties and average per capita income. Figure 2 shows the average per capita income for the five county groups based on effective buying income.[4]

The average per capita income in isolated rural counties is about one third of that in metropolitan counties. The income level rises sharply between isolated rural and isolated semirural counties, and between adjacent and metropolitan counties. Adjacent and isolated semirural county groups have about the same average income per capita.

In general, the same pattern of association between per capita income and the county group classification holds within individual states.

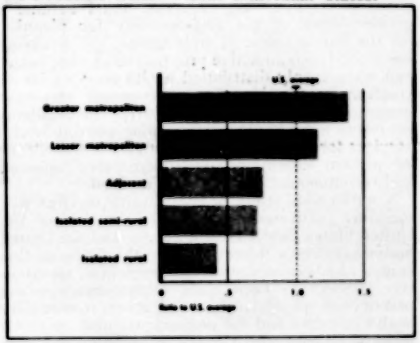

Fig. 2.—Average per capita income in the United States, by county group, 1940.

CHILD POPULATION, 1945

Since this study has been developed in order to determine health services currently available for children, it became necessary to have recent population data, at least for children. With the large shift in population during the war years, it was considered essential to determine the number of children county by county for 1945—figures which were not available elsewhere for this inter-census year.

2. The basis of this classification was furnished by Elliott H. Pennell and the staff of the United States Public Health Service.

3. For example, when the 100 counties in North Carolina are divided into 16 cells (4 by size of largest urban place times 4 by our county classification), the value of the coefficient of mean square contingency, c, is 0.76. The maximum value of c for a 4 by 4 table is 0.87.

4. This is based on estimates of effective buying income in 1940, made by Sales Management and published in Sales Management, 48:1 no. 8 (April 10) 1941. The estimates were made on the basis of money actually paid for goods and services, federal allotments, money paid out of savings and surpluses by business and financial institutions, plus the nonmoney income of farm and village residents. The income is gross income before taxes are paid. The estimate is based upon a formula devised by Sales Management. Per capita figures were computed on the basis of population as reported in the United States Census of 1940.

5. North Carolina may again be used as an example. When the 100 counties are divided into 4 income classes and 4 county groups, the value of c, coefficient of mean square contingency, is 0.71 in this 4 by 4 table.

A method was devised for estimating population under 15 years of age as of July 1, 1945 for each county in the United States.[6]

According to these estimates, there were 36,000,000 children under 15 years of age in the United States as of July 1, 1945. Table 3 shows that 13,000,000 children—37 per cent of the total—are in isolated counties.

TABLE 3.—*Children in the United States, by County Group, 1945*

	Children under 15	
	Number	Percentage
Greater metropolitan	8,374,609	23
Lesser metropolitan	8,635,100	24 } 63
Adjacent	5,837,352	16
Isolated semirural	9,659,071	27
Isolated rural	3,499,573	10 } 37
Total	36,005,795	100 100

It is this group of 13,000,000 children living in isolated counties with which we are particularly concerned in this discussion, for these are the children who are far removed from the health services and facilities of large urban centers. Children in these isolated counties do not have the same opportunities for medical care as do those children who happen to be living in more favored localities. Deficiencies appear in all aspects of health services and facilities: hospitals, physicians and dentists and community health services.

HOSPITALS, PHYSICIANS AND DENTISTS

Hospitals.—In surveying hospital facilities it has been impossible to obtain any count of the total number of beds used by children. Except in pediatric hospitals and those with separate pediatric units set aside exclusively for children, many beds are used interchangeably for children and adults according to need and circumstance. Therefore, for present purposes, we have based our calculations on the total number of beds[7] in all general hospitals which admit children, defining children as of the ages between birth and 15 years.

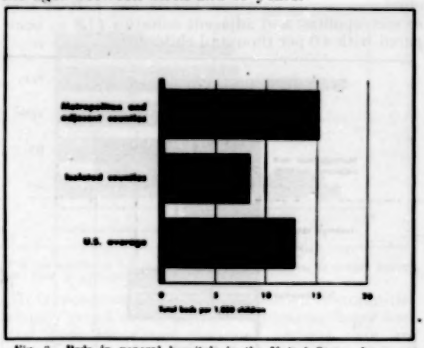

Fig. 3.—Beds in general hospitals in the United States, by county group, 1946.

In 1946, there were approximately 463,000 such beds in the United States, a ratio of 3.3 to 1,000 persons.[8] When related to child population, the ratio becomes 12.8 beds to every 1,000 children.

As shown in figure 3, the ratio in the service areas made up of metropolitan and adjacent counties is 15.4; in isolated counties, 8.4. Thus children in isolated areas have only about half the relative number of hospital beds available locally for their care as have the children in or near large urban centers.

Physicians.—Of all physicians in the United States in 1946, 116,000 were recorded as in private practice.[9] This number excludes retired physicians and those in full-time academic, administrative, research or institutional positions, and those employed by federal, state and local health agencies. For the country as a whole, the number of physicians in private practice in relation to population is 0.8 per 1,000 persons (1 practicing physician per 1,200 persons).[8] Relating the total number of practicing physicians to child population, the rate becomes 3.2 per 1,000 children.

6. Population under 5 years of age, as of July 1, 1945, was estimated for each county on the basis of the number of births for each of the five calendar years 1940 through 1944. Survival rates for each year of age were applied to the number of births occurring in each of the years. The rates used were those for each of the three major geographic regions of the United States and for white and nonwhite population separately in the South. The figures obtained by the application of survival rates to the births occurring in each of the five years 1940 through 1944 were added for each county, and these totals were corrected for under-registration of births. The county estimates of total living population under 5 years of age were then adjusted to tally with the estimated population of the entire United States under 5 years of age as of July 1, 1945. The number of children aged 5 to 14 years, as of July 1, 1945, was estimated for each county on the basis of changes in school enrollment since 1940. The ratio of elementary public day school enrollment as of June 1945 to that of June 1940 was used to project to 1945 the 1940 census population in this age group for each county. The county estimates of population were then adjusted to tally with the estimated population of the United States for the ages 5 to 15 years as of July 1, 1945. Child population under 15 years of age was obtained by combining these two estimates. Sources were as follows:
(a) Vital Statistics of the United States: II. Natality and Mortality Data for the United States Tabulated by Place of Residence, 1940-1944, United States Department of Commerce, Bureau of the Census, 1945.
(b) United States Abridged Life Tables, 1939: Urban and Rural, by Regions, Color and Sex, United States Department of Commerce, Bureau of the Census, unnumbered, (June 23) 1943.
(c) Studies in Completeness of Birth Registration: I. Completeness of birth registration, United States, Dec. 1, 1939 to March 31, 1940, United States Department of Commerce, Bureau of the Census, Vital Statistics, special reports 17: no. 18 (April 20) 1943.
(d) Estimated Population of the United States, by Age, Color, and Sex, 1945 and 1946, United States Department of Commerce, Bureau of the Census, Jan. 27, 1946, series p-46, no. 2.
(e) Data from State Departments of Education for School Years 1939-1940 and 1944-1945.
(f) Sixteenth Census of the United States, 1940. II. Population: Characteristics of the Population, United States Department of Commerce, Bureau of the Census, 1943.

7. Beds in general, maternity and pediatric hospitals, both those registered by the American Medical Association and those unregistered, provided that they: *(a)* report five or more beds and *(b)* admit at least 10 children or 10 obstetric cases annually. Beds in general hospitals operated by the Bureau of Indian Affairs are included on the assumption that they represent facilities operated on a local area basis, but other federal hospitals are excluded. Also in the excluded group are maternity nursing homes, hospitals in jails, prisons and reformatories, school hospitals and infirmaries and health camps.

8. Based on total population as of July 1, 1946. Child population by counties as of July 1, 1945, is used as the basis for rates by county group.

9. A list of physicians in private practice was prepared in each state on the basis of all available sources of information, including the American Medical Directory: II. Physicians, Chicago, American Medical Association, 1942; membership lists of the state and county medical societies; records of the Procurement and Assignment Service, of the State License Bureau, of the State Health Department and of the Internal Revenue District offices. Schedules, sent to each physician listed, asked, "Are you engaged in private practice? If NO, state reason." For those physicians failing to return schedules, information as to whether or not each was engaged in private practice was obtained through local health officers, state and county medical societies or by telephone or postcard. This inquiry also served to determine whether or not these physicians considered themselves as specialists. Thus a final corrected list of all physicians in private practice was obtained. It should be noted that there was no exclusion of physicians who do not treat children. The lists were prepared between April and December 1946, except in the following states: North Carolina (November 1945), Mississippi (January 1947), Oklahoma (March 1947) and Wyoming (July 1947).

When we analyze the physician-child ratio according to county groups, pronounced inequalities are revealed. In figure 4 it is seen that the physician-child rate in isolated counties is one half of that in metropolitan and adjacent counties (1.8 as compared with 4.0 per thousand children).

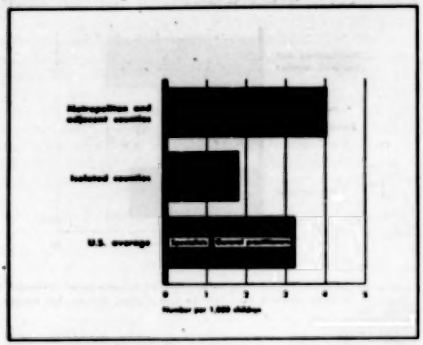

Fig. 4.—Physicians in private practice in the United States, by county group, 1946.

In analyzing the distribution of physicians, we should consider specialists and general practitioners separately. All physicians who reported that they limited their practice to a recognized specialty are defined as specialists. They tend naturally to concentrate in or near medical centers. The service areas around urban centers include 89 per cent of all specialists. The 13,000,000 children in isolated counties have relatively little specialist care available locally—0.3 specialists per thousand children as compared with over five times that rate (1.6) in the metropolitan and adjacent counties.

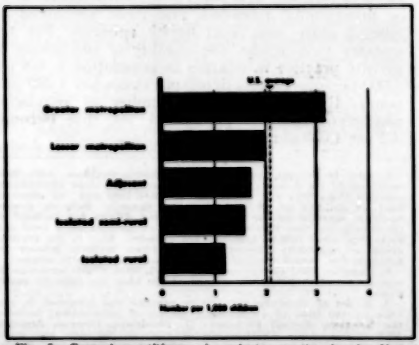

Fig. 5.—General practitioners in private practice in the United States, by county group, 1946.

All children should have equal opportunities to benefit from the highly skilled knowledge and technic of specialists. However, in a large proportion of cases, specialist care does not constitute an emergency. The child may be taken to the specialist or the specialist brought to the child, even though he lives far away in an isolated rural county.

In the case of the general practitioner, however, the situation is different. Just as many general practitioners are needed to care for 1,000 children in isolated rural areas as in the metropolitan areas. In fact it may be argued that more general practitioners are required in proportion to population in isolated areas, since the specialists are fewer and also distances are greater. The ratio of general practitioners is shown therefore for each of the five county groups in figure 5. There are 3.2 general practitioners for every 1,000 children in the greater metropolitan counties, but only 1.2 in isolated rural counties.

Dentists.—The scope of our study has included dental care for children. Dental caries shares with the common cold the unenviable honor of the commonest disease of children as well as adults. Any survey of child health services must therefore give serious attention to the distribution of dentists and the care they render to children.

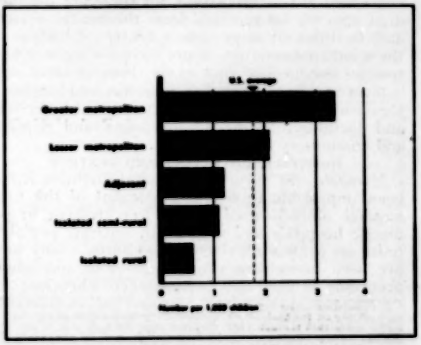

Fig. 6.—Dentists in private practice in the United States, by county group, 1946.

In 1946 about 66,000 dentists were reported in private practice in the United States.[10] Since our data do not show how many of these dentists accept children as patients, we have used the total number in relation to child population and, for the purposes of this discussion, have not separated specialists from those in the general practice of dentistry. As in the case of physicians in general practice, inadequacy of care and neglect of health results if dentists are not readily available. The rural child who must travel far to see a dentist gets inadequate dental care or none at all.

Figure 6 shows that there are 1.8 dentists per thousand children in the United States. In the isolated rural counties the rate is 0.6, or less than one fifth that in the greater metropolitan counties (3.4). Thus the distribution of dentists follows the same pattern as that of physicians, with a concentration in or near large urban centers. As in the case of the medical general practitioners, the rates in adjacent and in isolated semirural counties are nearly identical and much lower than in lesser metropolitan counties.

10. A list of dentists in private practice was prepared in each state using similar methods to those described for physicians in footnote 9. The lists were prepared between April and December 1946, except in the following states: North Carolina (January 1946), Indiana (January 1947), Mississippi (January 1947), Oklahoma (March 1947) and Wyoming (July 1947).

DEFICIENCY IN HOSPITAL BEDS, PHYSICIANS AND DENTISTS IN ISOLATED COUNTIES

A graphic summary of the deficiency in hospital beds, physicians and dentists in relation to the population in the isolated counties is shown in figure 7. About one third of the total population

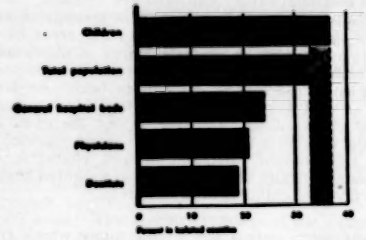

Fig. 7.—Summary for isolated counties in the United States.

live in these isolated counties.[11] Locally available to this third of the population are 24 per cent of the hospital beds, 21 per cent of the physicians and 19 per cent of the dentists. As shown in figure 7, the gap between the lengths of the columns for hospital beds, physicians and dentists and that for total population is an indication of the deficiency in these three categories of health services.

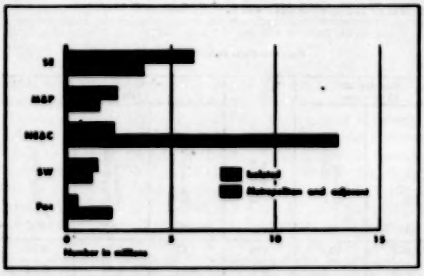

Fig. 8.—Summary for regions in the United States, by county group, 1946: children.

In respect to children, the deficiency is even greater. Rural families are on the average larger than those in cities, so that in these isolated counties the proportion of children is relatively greater. The 13,000,000 children in the isolated counties, who constitute 37 per cent of the children of the United States, get distinctly less than their share of the service of hospitals, physicians and dentists located in their own areas.

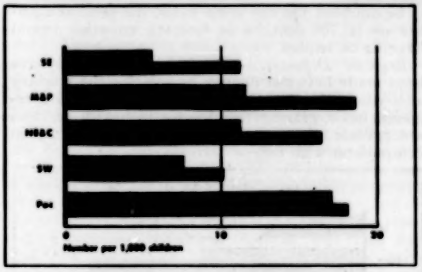

Fig. 9.—Summary for regions in the United States, by county group, 1946: beds in general hospitals.

It is recognized that sparsely settled communities actually require within their boundaries fewer hospital beds for every thousand persons than are needed in cities. In cities, with their medical centers, specialists and highly skilled professional services, hospitals not only serve the patients among their own urban populations, but also admit for diagnosis and treatment many of the patients with more difficult cases referred from nonurban areas. This difference in the number of beds required in urban areas as compared with rural areas has been taken into account in the standards recommended by the United States Public Health Service. On the basis of their proposed allotments among hospital districts, it is estimated that the number of general beds in isolated counties would have to be increased by at least 50 per cent.[12]

In respect to physicians and dentists, serious deficiencies exist in isolated areas. It has already been stated that isolated counties need as many,

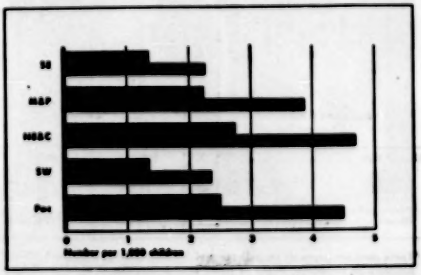

Fig. 10.—Summary for regions in the United States, by county group, 1946: physicians.

if not more, general practitioners for every 1,000 persons as are needed in the greater metropolitan counties if children in these counties are to have equal opportunity for medical care and health supervision. In order to assure that children in isolated counties have available to them in their own areas general practitioners at a rate available to

11. Although, as indicated previously, estimates of child population for each county as of July 1, 1945 were made in connection with this study, no corresponding estimates were practicable for the population of all ages. Tabulation of data from the 1940 Census, however, show that 33 per cent of the total population and 35 per cent of the children live in isolated counties:

	Children Under 15	Total Population
Greater metropolitan	7,565,504	38,402,167
Lesser metropolitan	7,291,471	31,813,041
Adjacent	5,442,993	20,284,894
Isolated semirural	9,125,551	31,569,042
Isolated rural	3,556,568	11,170,141
Total	32,972,081	131,669,275

12. Based on a special tabulation of the data, in Mountin, J. W.; Pennell, E. H., and Hoge, V. M.: Health Services Areas—Requirements for General Hospitals and Health Centers, Public Health Bulletin no. 292, Federal Security Agency, United States Public Health Service 1945.

the children in the greater metropolitan counties of the United States, the present count of 19,600 general practitioners in these counties would have to be doubled. On the same basis, the present number of 12,700 dentists in isolated counties would have to be tripled.

Regional Differences.—So far comparisons have been made between county groups for the country as a whole. If now the country is divided on a regional basis, glaring deficiencies in health services are revealed in some sections of the country in comparison with others.

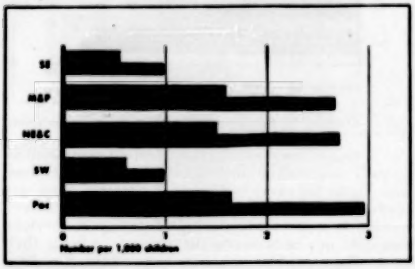

Fig. 11.—Summary for regions in the United States, by county group, 1946: dentists.

For the purpose of this study the states have been grouped into five regions. Without attempting to give a full description of regional differences at this time, we may call attention to certain deficiencies in the Southeast region. This is an area which is predominantly rural, with a large proportion of the country's rural children. In our group of isolated counties in the Southeast region, there are 6,000,000 children—almost half of the total 13,000,000 children of the United States living in isolated counties (fig. 8).

These isolated counties in the Southeast region show the lowest rates of general hospital beds, physicians and dentists of any of the five regions presented in figures 9, 10 and 11. Hospital facilities are available at a rate only half of that for metropolitan and adjacent counties in the same region. Children in isolated counties in the Pacific region, the region with the highest rate, have three times as many hospital beds per child. Discrepancies of about the same magnitude are apparent for physicians and for dentists.

When a comparison of facilities and personnel is made state by state, the lowest rates are usually found in the twelve states of the Southeast region (table 6).

Community Health Services.—It is sometimes assumed that, although children in rural areas have less than their share of the services of physicians in private practice, this is at least in part compensated by an increase in community health services such as well-baby clinics, public health nurses and dental clinics. Such, however, is not the case. In fact the reverse is true. We have already reported [13] that the amount, distribution and character of community health activities are also weighted heavily in favor of children in urban areas.

CONCLUSION

These facts, only a few of the many which are being sharply defined by the Academy's study, reveal in specific detail inequalities in the amount of medical care received by children in rural areas. Children living in these areas are handicapped particularly in specialist care, clinic care and the highly skilled diagnostic and treatment services received in hospitals—those very services which have been agreed on as the right of every child.

Now that the facts have been obtained, the American Academy of Pediatrics, with the continuing cooperation of the United States Public Health Service and the United States Children's Bureau, has undertaken an action program for the improvement of child health not only for the country as a whole but for every state, county and local community. The field is limitless in its scope, but already certain specific projects have been planned. Most prominent among the projects for first consideration are: (1) to strengthen pediatric teaching in order

Table 6.—*Child Population, Beds in General Hospitals and Private Practitioners, by State and County*[a]

State and County	County Group	Population, 1945	Beds in General Hospitals, 1946	Private Practitioners, 1946					
				Number of physicians			Number per 1,000 children		
		Children Under 15	Number	Total	General Practitioners	Number of Dentists	Physicians	General Practitioners	Dentists
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
ALABAMA	X	992,741	5,653	1,382	931	545	1.37	0.94	0.55
Autauga	3	7,075	18	5	5	1	0.71	0.71	0.14
Baldwin	3	12,027	50	17	13	6	1.33	1.01	0.47
Barbour	3	11,270	28	11	11	3	0.98	0.98	0.27
Bibb	3	7,075	0	7	6	2	0.99	0.85	0.28
Blount	3	10,136	24	6	6	2	0.59	0.59	0.20

[a] These data are given as an indication of the data available for each county in the United States. The full table can be obtained on request to the American Academy of Pediatrics, Study of Child Health Services, 2316 Massachusetts Ave., N. W., Washington 8, D. C.

13. Williams, C. L., Jr.; Hubbard, J. P., and Bain, K. Community Health Services in Eight Selected States, Am. J. Pub. Health 38:75-81 (Jan.) 1948.

to provide more physicians who are well trained in the medical care and health needs of children, especially in remote areas, and (2) to develop and implement recommendations made by state and local communities in order to provide better and more evenly distributed health services for all children, particularly in rural areas where adequate services are now deficient.

AORTIC PULMONARY ANASTOMOSIS IN CONGENITAL PULMONARY STENOSIS

Report of Forty-Five Cases

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and
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In November 1946, Potts, Smith and Gibson [1] reported a new surgical procedure for the relief of congenital pulmonary stenosis. The operation consists of a direct anastomosis between the aorta and a pulmonary artery. The use of the aorta was made possible by the invention of a clamp which permits blood to flow through this vessel while the anastomosis is being performed. This technic differs from the Blalock and Taussig [2] method only in the fact that the aorta itself rather than one of its branches is used to direct additional blood to the lungs.

Anastomosis between the aorta and a pulmonary artery has been performed on 45 patients, and in addition 7 patients have been explored in whom the anastomosis was not undertaken. We shall first discuss the criteria used in the selection of these patients for operation.[3]

DIAGNOSIS

In 48 of the 52 patients submitted to operation, the preoperative diagnosis was the tetralogy of Fallot. This syndrome is by far the most frequent condition in which the circulation to the lungs is inadequate. It consists of pulmonary stenosis, defect of the interventricular septum, aorta overriding the septal defect and hypertrophy of the right ventricle.

The characteristic clinical picture is that of a patient who is cyanotic, especially about the eyes, nose, mouth and tips of the fingers and toes. The eyes are suffused. The fingers and toes are clubbed. The patient is usually unhappy and irritable, and the state of nutrition is often poor. In some instances there is retardation in mental development. Physical examination reveals the heart to be normal in size or only slightly enlarged, with a systolic murmur best heard along the left sternal margin at about the second or third left interspace. Roentgenologic examination shows a heart that is boot shaped, the apex being blunt and rounded and the heart appearing to lie more or less transversely in the chest. The pulmonary fields show little vascularity. Fluoroscopic examination fails to reveal pulsations in the hilar regions, and in the left anterior oblique position the pulmonary window is abnormally clear. The electrocardiogram is characterized by pronounced axis deviation to the right. The red cell count and hemoglobin are elevated. The arterial oxygen saturation is diminished.

Such is the classic picture of the tetralogy of Fallot, and under such circumstances the diagnosis can be made with confidence. There are, however, many variations from this typical pattern, and on this account we shall discuss briefly a number of the diagnostic points which have been mentioned.

The degree of cyanosis varies widely. In some of the children, cyanosis was scarcely noticeable when the patient was at rest. There was likewise a wide variation in the red cell count and hemoglobin. In our series the red cell count varied between 5,000,000 and 10,000,000. Nor was there as close correlation between the red cell count and hemoglobin as one might expect. Moreover, the degree of cyanosis, the number of red blood cells or the amount of hemoglobin did not necessarily show a close relationship to the patient's limitation of activity. Some who were decidedly cyanotic with high red cell counts and hemoglobin were able to walk several blocks before becoming breathless. Others, who from their general appearance and blood examination would appear to be less severely handicapped, were able to walk only a few yards. The inability to exercise would seem to be the most important criterion in deciding whether operation is urgently indicated.

Examination of the heart usually reveals a systolic murmur which is best heard along the left sternal margin at about the second and third interspaces. Sometimes it is long, harsh and rasping, while in other instances it is short and of slight intensity. A thrill may or may not be palpable. Absence of a murmur is a cause for anxiety. Operation has been performed on 2 children in whom no murmur could be detected. In 1 a satisfactory anastomosis was completed, and the patient made an uneventful recovery. In the other, the pulmonary artery was too small to allow the anastomosis to be effected, and the patient failed to survive the exploration.

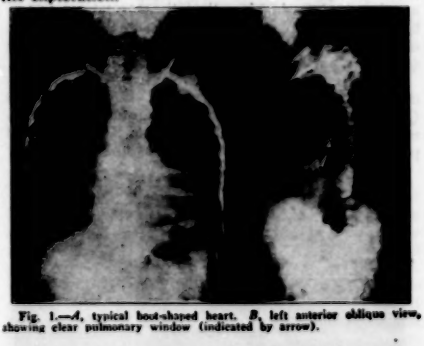

Fig. 1.—*A*, typical boot-shaped heart. *B*, left anterior oblique view, showing clear pulmonary window (indicated by arrow).

Autopsy revealed the characteristic features of the tetralogy save that pulmonary atresia rather than stenosis was present. A large interventricular septal defect was present, but in this instance at least, its presence had not resulted in an audible murmur. It is our belief that the first of these 2 patients also had pulmonary atresia, but was fortunate in that the pulmonary branches were sufficiently large to allow the anastomosis. Failure to hear a murmur should put one on his guard both as to diagnosis and prognosis, in the event that operation is decided on.

Roentgenologic study is perhaps the most important single feature of the examination. A 2 M. roentgenogram of the chest in the anteroposterior position almost

From the Children's Memorial Hospital.

1. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of the Aorta to a Pulmonary Artery for Certain Types of Congenital Heart Disease, J. A. M. A. 132:627-631 (Nov. 16) 1946.

2. Blalock, A., and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There Is Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. 128:189-202 (May 19) 1945.

3. In this connection we wish to state that Dr. Helen Taussig and her co-workers at the Johns Hopkins Clinic have taught us much in our frequent visits there.

always reveals a heart that is normal in size or only slightly enlarged. Gross cardiac enlargement militates strongly against the diagnosis of the tetralogy of Fallot. In no case in our series has the heart been estimated as more than 25 per cent enlarged.

The shape of the heart is subject to considerable variation. It is gratifying if the roentgenogram shows a heart that is boot shaped, appearing to ride high on the diaphragm, lying more or less transversely in the chest (fig. 1 *A*). However, the heel of the boot is often inconspicuous, and the heart may be found in its normal position with little blunting of the apex. In several instances our roentgenologist has pronounced the heart to be of normal size and shape. A slight concavity is usually present in the pulmonary area, or the contour may appear normal. Prominence in the region of the pulmonary conus indicates a large pulmonary artery and should immediately cast doubt on the diagnosis of the tetralogy of Fallot. The appearance of the hilar regions must also be noted. If there is evidence of increased vascularity, it is an important sign that the lungs are receiving a sufficient amount of blood.

Fluoroscopic examination is important in determining the amount of blood flow through the pulmonary arteries. With the eyes thoroughly accommodated search should be made for expansile pulsations in the hilar regions. Absence of pulsations is the rule in pulmonary stenosis. Their presence means that the flow of blood to the lungs is adequate. Fluoroscopic study of the patient in the left anterior oblique position is obligatory. In this position one is able to determine whether there is an abnormally clear area beneath the aortic arch; in other words, whether the pulmonary arteries are carrying less than the normal amount of blood. An abnormally clear pulmonary window is one of the most reliable signs of pulmonary stenosis (fig. 1 *B*).

The electrocardiogram usually shows an extreme degree of axis deviation to the right. In most instances QRS_1 is practically altogether downward with QRS_2 upright. P waves, particularly in lead 2, are high and pointed (fig. 2 *A*). Once the diagnosis of the tetralogy

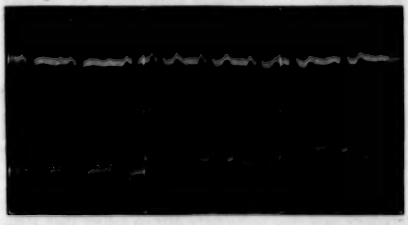

Fig. 2.—*A*, axis deviation to the right in tetralogy of Fallot. *B*, axis deviation to the left in tricuspid atresia.

of Fallot has been made, it is still necessary to determine the position of the aortic arch before operation is undertaken. In 15 to 20 per cent of cases, the aorta descends on the right. In order to do the anastomosis one must enter the chest on the side on which the aorta lies. In our series a right aortic arch was encountered in 7 instances.

The position of the arch can often be determined by simple inspection of the anteroposterior roentgenogram of the chest, particularly when it lies on the left. The aortic knob and the descending aorta may be well outlined. In other cases, one must use a barium swallow, and observe under the fluoroscope the deflection of the barium to the right or left. Indentation of the esophagus on the left indicates a left arch, and vice versa. In a number of young, uncooperative patients, we have found it helpful to administer a thick barium mixture with the patient lying supine and the foot of the fluoroscopic table elevated. A roentgenogram is made just after the patient has swallowed (fig. 3). In

Fig. 3.—*A*, barium-filled esophagus with indentation on left indicating left aortic arch. *B*, indentation on right indicating right aortic arch.

this way, the entire course of the esophagus can frequently be well outlined. (Some confusion has arisen from the use of the terms "dextroposition of the aorta" and "right aortic arch." Dextroposition of the aorta refers to the position of the aorta at its origin, and

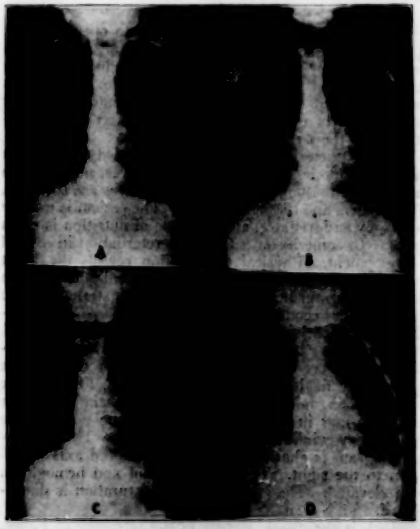

Fig. 4.—Anteroposterior roentgenograms of the 4 patients in whom a diagnosis of tricuspid atresia was made.

means that the aortic orifice is shifted to the right, overriding the accompanying interventricular septal defect and thus arising from both ventricles rather than the left ventricle alone. Dextroposition of the aorta is an integral part of the tetralogy of Fallot and carries no implication as to the position of the aortic arch, which may be either on the right or left.)

In 4 of the patients who came to operation, the clinical diagnosis was tricuspid atresia. A number of other characteristic defects usually accompany this lesion: namely, interauricular septal defect, defect of the interventricular septum, rudimentary right ventricle and hypoplasia of the pulmonary artery. The course of the flow of blood from the right auricle is as follows: through the interauricular septal defect into the left auricle, thence to the left ventricle, where a portion of the mixed blood from the left ventricle passes through an interventricular septal defect into the diminutive right ventricle and on into a more or less narrowed pulmonary artery.

The physical signs are identical with those encountered in the tetralogy of Fallot. There are the same cyanosis and clubbing, the same findings with respect to the blood and the same systolic murmur over the precordium. There are, however, two important features which serve to distinguish tricuspid atresia from the tetralogy. The roentgen silhouette in the anteroposterior view shows a gentle rounding of the left cardiac border due to hypertrophy of the left ventricle and an absence of the normal fulness of the region of the right ventricle (fig. 4). The second diagnostic feature is axis deviation to the left in the electrocardiogram (fig. 2*B*). These features were present in all 4 of our patients. Three of the patients had a pulmonary artery sufficiently large to permit a satisfactory anastomosis, and all 3 made a satisfactory recovery with striking improvement. In the fourth case, the pulmonary artery was rudimentary, and no anastomosis could be done. The patient survived the exploratory operation.

In some cases of tricuspid atresia, there is no communication between the two ventricles and blood must reach the lungs by way of a patent ductus arteriosus. Such was not the case in any of our 4 patients. Inasmuch as the anastomosis is done in the immediate vicinity of the ductus, the question of its patency can be determined by inspection during the operation.

OPERATION

From Sept. 13, 1946 to Aug. 15, 1947, aortic pulmonary anastomosis for relief of cyanosis due to congenital pulmonary stenosis has been performed on 45 patients. In addition, 7 patients were explored.

Although the technic of operation remains substantially the same as originally outlined, emphasis on important steps, clarification of misunderstood points and a description of slight modifications in technic will be reviewed.

In addition to careful selection of patients suitable for operation, skilful anesthesia is essential for operative success. The rather severe grades of anoxemia allow these patients a narrow margin of safety over which an expert anesthetist must carry them. Without the services of a well trained anesthetist, capable of giving intratracheal anesthesia, resourceful in emergencies and conscious of the significance of the slightest change in pulse, respiration and blood pressure, the mortality will rise appreciably. In no operation is the work of the anesthetist more important.

The child is placed in a lateral position on the operating table and the chest is entered through a posterolateral incision in the left fourth interspace if the arch of the aorta curves normally to the left (fig. 5*A*). In case of a right aortic arch the incision is made in a similar manner on the right side.

Identification of the right or left pulmonary artery is usually not difficult. In some cases it is small and buried in masses of small tortuous thin-walled veins and fibrous tissue. Since the loss of blood is less hazardous to these plethoric children the veins are dissected from the pulmonary artery with a fair degree of confidence. The large veins are tied with fine silk; bleeding from the tiny veins is disregarded.

We use no sponges in the chest. The blood is lavaged away from the operative site with a stream of isotonic solution of sodium chloride removed with an aspirator. The chloride solution, delivered with an ordinary 50 cc. bulb syringe, not only is nontraumatic, but also is effective in removing the dark blood caught in the meshes of adventitia, thus making important structures identifiable.

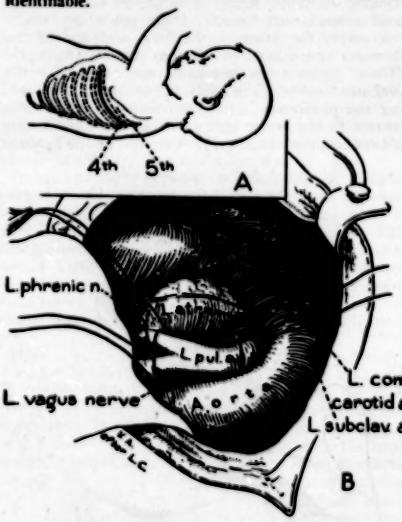

Fig. 5.—Technic of aortic pulmonary anastomosis.

There is considerable variation in the size, length and branching of each pulmonary artery. The average size is between 5 and 8 mm. in diameter. The pulmonary artery was approximately 4 mm. in diameter in 5 patients on whom successful aortic pulmonary anastomoses were performed. Not infrequently the pulmonary artery is embedded in dense fibrous tissue and appears very small, but after complete dissection and removal of excess adventitial tissue, expands considerably. In 1 patient the pulmonary artery was actually 18 mm. in diameter, measured with a caliper, twice the size of the adjacent aorta. The intrapulmonary pressure was practically zero and a successful anastomosis was performed with good results.

The left pulmonary artery is longer than the right and usually does not break up into branches before entering the hilus of the lung as does the right. The left pulmonary artery lies fairly near the aorta and courses in almost the same plane, whereas the right pulmonary artery lies near the inferior portion of the hilus of the lung and courses in a plane almost perpendicular to the aorta. It was feared that anastomosis of a pulmonary artery to an aorta lying at right angles

to it would result in kinking and obstruction of the newly formed channel. This has not been true in 7 patients in this series who had right aortic arches and on whom successful anastomoses were performed. The pulmonary artery is very elastic and easily adjusts itself.

Worries about intrapulmonary pressure are for the most part needless. By observation of partial or complete absence of pulsations in the pulmonary artery and by palpation of the faintly beating vessel it is possible in most instances to decide promptly that the intrapulmonic pressure is below normal. If any question arises, the pressure can be determined easily by a simple water manometer consisting of a needle attached to rubber tubing to a calibrated pipet.

Doubly encircling ligatures of no. 00 oiled silk are placed around each branch of the pulmonary artery as it enters the hilus of the lung and around the pulmonary artery as far proximal as possible (fig. 6*A*).

These ligatures are laid aside until ready for the actual anastomosis. The method of temporarily obliterating the pulmonary artery and fixing it with these ligatures to the aortic clamp during the anastomosis has been modified (fig. 6*A*). One end of the ligature

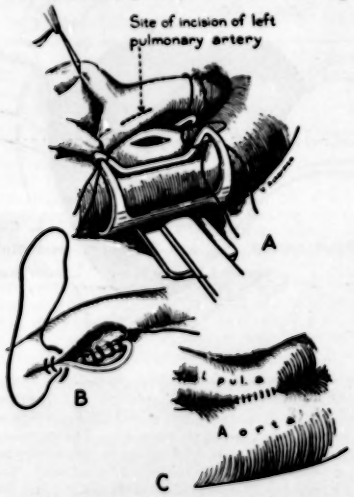

Fig. 6.—Technic of aortic pulmonary anastomosis.

doubly encircling the distal branch of the pulmonary artery lying nearest the aortic clamp is threaded through the posterior flange of the distal portion of the clamp in one direction and through the anterior flange in the opposite direction. The other end of this same ligature is threaded through the flanges of the clamp in the opposite direction. The ends of the ligature are then drawn up snugly to appose the pulmonary artery to the aorta in the best possible position for anastomosis and tied just tightly enough to occlude but not injure the vessels. The ligature around the proximal portion of the pulmonary artery is attached to the flanges of the other end of the clamp in the same manner.

There have been no changes in the aortic clamp. It is made in three sizes, small, medium and large. The medium-sized clamp is used for most patients. For children below 1 year of age, and for a few older children with rather small aortas, the small-sized clamp was used. The large clamp was used on 2 rather large children, both aged 12. It is imperative after the clamp is applied to the aorta and closed that a thrill be palpable in the aorta distal to the clamp in order that sufficient blood flow to the spinal cord is assured.

The site of anastomosis to the aorta is determined by the position of the pulmonary artery. This point is usually about 2 cm. distal to the origin of the subclavian artery.

The length of the incision in the aorta and pulmonary artery has been the subject of much discussion and concern. The desirable size of the final anastomotic channel will be dealt with later.

The technic of continuous, over and over suture with no. 5-0 Deknatel silk has not been changed (fig. 6*B*)

On completion of the anastomosis and release of the ligatures and clamp, there has been in each case a continuous palpable thrill over the site of the new channel, indicating that blood was flowing through (fig. 6*C*). In 3 patients one extra stitch was necessary to stop bleeding from the suture line.

On completion of the operation the lungs are carefully and fully expanded. In the sixth intercostal space a small stab wound is made in the chest and a de Pezzer catheter, so cut as to leave only a flange, is pulled through the chest wall from the inside out to provide drainage. The ribs are apposed with two heavy catgut sutures encircling adjoining ribs. The periosteum is dissected from the lower margin of the rib at the point where the catgut is to be introduced so as to avoid pressure on the intercostal nerve. The muscle layers are closed with running surgical gut sutures and the skin with silk.

The child is returned to its room and placed in an oxygen tent for a day or two. The chest drain is connected with a water seal and left in the chest three days. Penicillin, 30,000 units every three hours, begun two days before operation, is continued after operation for seven to ten days routinely.

Postoperative complications have been few. One or two aspirations of fluid and/or air from the chest were necessary in 4 patients. All occurred in the early cases before it became routine to place a drain in the chest at the close of operation. Severe tracheobronchitis with laryngeal edema necessitating tracheotomy occurred in 2 patients. Three patients had mild tracheobronchitis which was relieved by a day or two in the steam room. One of these children had an associated collapse of the upper lobe of the left lung which reexpanded without difficulty. Cerebral anoxia in 1 patient caused total paralysis for three days. Recovery was complete. The average period of hospitalization after operation was fifteen days.

MORTALITY

Aortic pulmonary anastomosis has been performed on 45 patients, of whom 4 died, a mortality of 8.8 per cent (the table). Of 10 children in the first group, 3 were below 1 year of age—4, 6 and 8 months respec-

Mortality Statistics

Ages	Number of Patients	Deaths	Mortality, Percentage
4 mo. to 2 yr.	10	1	10
2 to 5 yr.	19	2	10.5
5 to 13 yr.	16	1	6.3
Total	45	4	8.8

tively. In the first 11 patients operated on there were 3 deaths; in the next 34 patients there was 1 death.

The first death, in a child aged 11 years, previously reported, was due to cerebral thrombosis. She had had hemiplegia since infancy. The second death, in a child aged 1.5 years, was likewise due to cerebral thrombosis. This child also had had a cerebral accident four months before operation. The third death, in a child aged 2.5 years, was due to postoperative shock and tension pneumothorax consequent to apical tuberculosis unrecognizable preoperatively. These 3 children died within twenty-four hours after operation. Hemorrhage into the hypothalamus was the cause of the fourth death, which occurred three days after operation.

Seven operations proved to be exploratory only. One child had an unrecognized Eisenmenger complex not remediable by surgery. The other 6 were hopeless from a surgical point of view because only strand-like pulmonary arteries carrying no blood were found at operation. Three of this group of 7 failed to survive the unavoidable increased anoxemia attendant on opening the chest. In fact, 2 died on the operating table and the third died in two days without regaining consciousness. Two of these children were in no worse condition preoperatively than many in the previous group on whom an anastomosis could be performed and who made uneventful postoperative recoveries. The third was a very poor surgical risk. Postmortem findings in all were essentially similar, confirming the operative diagnosis of undeveloped nonfunctioning pulmonary arteries due to pulmonary atresia. Bronchial arteries arising from the ascending and descending portions of the aorta were the only carriers of blood to the lungs.

Considering the patients who died after exploration only, in contrast with patients in similar preoperative condition who survived aortic pulmonary anastomosis, this observation presents itself: The child who has a pulmonary artery suitable for anastomosis has postoperatively an increased flow of blood to the lungs and can survive the shock of an open chest and temporary occlusion of a pulmonary artery, whereas the child who has an inadequate pulmonary artery and consequently cannot receive the benefit of anastomosis and increased blood flow to the lungs withstands the shock of an open chest poorly.

COMMENT

Of 41 patients who survived surgery, 39 have been tremendously improved; i. e., they are relieved of cyanosis, have gained weight and are able to live fairly normal lives. Two patients are improved; their cyanosis is only partially relieved and on exertion they still become somewhat cyanotic. It is only a year since the first child was operated on, so that no conclusions can be drawn as to ultimate prognosis. No child has died since discharge from the hospital. To date endocarditis has not developed postoperatively. That the anastomotic channels are remaining open and functioning is known from the persistence of a soft systolic and diastolic humming top murmur heard in all children examined and from the fact that cyanosis has not recurred.

Selection of patients for operation has been on the basis of diagnosis alone. No child has been refused surgical treatment regardless of a seemingly hopeless prognosis if the preoperative diagnosis indicated a decreased flow of blood to the lungs probably remediable by surgical treatment. Six of the patients operated on were in such a severe state of anoxia that they could barely sit up in bed, and 3 had to have intermittent or continuous oxygen. Anastomosis was possible in all these children, and oddly enough all survived.

It must be appreciated that children who have had an aortic pulmonary anastomosis for pulmonary stenosis have not been restored to normal. The basic pathologic condition remains in their hearts and extra work is added by the creation of an artificial ductus arteriosus. However, the children are comfortable and happy and their mothers have been relieved of constant anxiety.

The average preoperative red blood cell count was 7,930,000. Two weeks after operation it had fallen to 5,620,000. The hematocrit reading dropped from an average of 64.4 per cent preoperatively to 51 per cent two weeks after operation. The oxygen saturation level of arterial blood was raised an average of 30 per cent. The greatest change was in the tolerance of exercise. Before operation many children were unable to walk more than a few yards. After operation they could walk as far as their undeveloped legs would carry them. Some of the clubbing of the fingers and toes disappears during the first two weeks after operation, and the balance is gone by four to six months.

It has not been possible to follow all the children postoperatively because many live far from Chicago. In those that have been followed there has been in every instance some enlargement of the heart. This enlargement has not been progressive but seems to become fixed within a month or two. In 3 children there has been pronounced enlargement of the heart. No signs of heart failure have developed but we are fearful that they may appear in the relatively near future.

How large should the anastomotic channel be made? Should it be smaller in a 1 year old than in a 12 year old child? Will the opening grow larger as the child grows? The final answer to these important questions awaits years of clinical experience and further experimental work. The objective sought is a ductus large enough to divert sufficient blood to the lungs to relieve cyanosis but not so large as to cause undue cardiac strain. Originally, we decided on $\frac{3}{16}$ inch (8 mm.) as the proper length for the incisions in the aorta and pulmonary artery. Obviously the length of the incision is not the diameter of the final opening. By multiplying $\frac{3}{16}$ inch (8 mm.) by 2 and dividing by 3.1416 we arrive at the final diameter of the newly formed ductus, or slightly less than $\frac{1}{8}$ inch (5 mm.). All measurements are made with a caliper.

Recently we shortened the incisions to $\frac{1}{4}$ inch (6.3 mm.), thus forming a final anastomotic channel of approximately 4 mm., or slightly less than $\frac{1}{6}$ inch, in diameter. When one is dealing with structures which vary in elasticity and thickness it is improper to assume that mathematical accuracy is possible. Furthermore, accuracy of suturing, especially at the corners, is a large factor in determining the size of the newly formed ductus arteriosus.

SUMMARY

Essential points in the diagnosis of the tetralogy of Fallot and tricuspid atresia are discussed. Important features of the technic of aortic pulmonary anastomosis are reviewed. Aortic pulmonary anastomosis has been performed on 45 patients with 4 deaths, or a mortality of 8.8 per cent.

GUEST PASSENGER INJURIES

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Accidental injuries to occupants of the front seat of automobiles are so typical that they can be classified into two groups. The injuries sustained by the driver have become known as "steering post injuries" and those sustained by others in the front seat are classified as "guest passenger injuries."

Steering post injuries are caused by sudden stops when the driver is forced against the steering wheel. Frequently the chin is lacerated, the mandible may be fractured, and in more severe injuries the maxilla and nose may be involved. Chest, knee and ankle injuries are also common.

Drivers nevertheless occupy the safest seat in the car; protected by the steering wheel, they escape injury in many severe accidents.

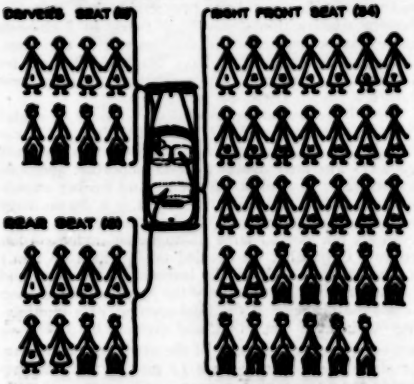

Fig. 1.—This chart shows the position in the car of 50 consecutive persons that committed me for treatment of facial injuries. Eight were drivers; 8 were in the rear seat; 34 were in the guest passenger seat. Twenty-five of these were women.

"Guest passengers" in the front seat beside the driver are on the contrary in the most dangerous seat in the car because of their unprotected position in case of sudden stops. Children sitting on mothers' laps or standing in the front are frequently injured and occasionally killed when sudden stops cause crushing injuries on the dashboard. Occupants of the "death seat" are injured in the proportion of about 3 to 1, as compared to drivers (figs. 1 and 2). Some years ago I investigated 50 consecutive patients with facial injuries from automobile accidents who came to the clinic for plastic surgery. About 70 per cent were young girls and women who had been riding beside the driver in the front seat. They had various types of "guest passenger" injuries (fig. 1).

Fig. 2.—Three typical types of guest passenger injuries: Type 1. The head is thrown up forward breaking the windshield; head and neck cuts usually result. Type 2. Combination windshield cuts and crushing facial injuries result from these glancing blows. Type 3. Crushing and tearing injuries result from contact with gadgets on the instrument board.

With the advent of better roads and high speed transportation, guest passenger injuries are becoming even more numerous and severe, and deaths more common. To determine more accurately the seriousness of the problem, I secured the cooperation of Inspector Louis J. O'Brien, head of the Accident Prevention Bureau of the Detroit Police Department, who kept a record of all the passenger car accidents involving personal injuries during September 1947. These statistics support former conclusions (as derived from a study of figure 1) and show an even more serious picture from the passenger's standpoint (table 1).

TABLE 1.—*Comparison of Injuries to Drivers and to Passengers in Private Passenger Cars, September 1947**

Accidents 444	Cars Involved 480		Injured 633
	Number Cars	Drivers Injured	Passengers Injured
Driver Alone	178	178	---
Driver with Passengers	13	13	0
	219	0	260
1. Passenger	168	52	159
2. Passengers	42	15	81
3. Passengers	44	11	71
4. Passengers	15	2	36
5. Passengers	9	2	20
6. Passengers	3	1	11
7. Passengers	1	0	4

*Compiled from a report of the Accident Prevention Bureau, Detroit Police Department.

According to Detroit traffic engineer surveys, in normal traffic, in 61 per cent of cars the driver was alone. No one had ever kept statistics (so far as I can determine) on the number of cars involved in accidents that were driven alone. This information was vital in the study of the guest passenger problem and therefore was considered in the one month survey made for me by Inspector O'Brien.

The One Month Survey of Accidents

This survey shows that in 178 of 480 cars, 37 per cent, the driver was the sole occupant (table 2). One hundred and forty drivers suffered body injuries; 85 head injuries, and 36 injuries to both body and head.

From the Straith Clinic for Oral and Plastic Surgery.

A startling contrast is shown by the fact that in 219 accidents involving multiple occupants, 260 passengers but no drivers were injured! There were only 13 accidents in which drivers were injured but passengers remained unharmed, [1] (table 1).

These figures emphasize the great danger to passengers in the "death seat" and the need for better interior design in automobiles to reduce this hazard.

TABLE 2.—*Comparison of Injuries as Related to Location in Car**

	Total Injuries	Head Injuries	Body Injuries	Both Injuries
Drivers	261	85	140	36
Passengers in front	248	99	122	27
Passengers in rear	124	42	67	15

*Compiled from a report by the Accident Prevention Bureau, Detroit Police Department, on injuries sustained in private passenger car accidents, September 1947.

Since this study is devoted especially to injuries of guest passengers occupying the front seat, it is noted that 372 persons were injured in 289 cars carrying passengers. Two hundred forty-eight, or 69 per cent, of these were riding in the front seat. More than one half of these suffered head injuries. It is this group that I wish to refer to in particular.

Head Injuries

Head injuries are caused when the passenger is thrown forward: (*a*) into the windshield (type 1); (*b*) into the windshield, the head being deflected downward on the dash (type 2); (*c*) directly against the dash (type 3) (fig. 2).

Fig. 3.—This guest passenger's head was forced through the windshield and the nose and upper lip were almost severed. Front and profile views show patient after scar excisions and insertion of preserved cartilage transplants to rebuild the nose.

1. The complete detailed police report will be furnished by me on request.

Type 1.—The head frequently crashes through the windshield and the face comes in contact with jagged glass. Almost complete decapitation has been known to occur in this type. Forehead injuries are numerous and cuts in the upper and middle third of the face are most common (fig. 3). Frequently the nose is severely lacerated or a portion may be severed. Portions of the forehead, cheek or ears may be similarly detached by jagged glass.

Fig. 4.—Type 2 injury. In this car the guest passenger was riding in a funeral procession at 20 miles per hour. A sudden stop caused her head to hit the windshield, cutting her forehead and causing her nose to be cut and crushed on the sharp edge of the dash.

Type 2.—Glancing blows from the windshield to the dash often cause both cutting and crushing injuries. Excessive speed is not always a factor, as evidenced by the patient who was riding in a funeral procession at the rate of only 20 miles (32.2 kilometers) per hour (figs. 4 and 5). Knobs, cranks, sharp ledges, etc., on the dash often do considerable damage in this type. Teeth are frequently dislodged in children and adults and many facial lacerations sus-

Fig. 5.—This patient hit the windshield and came down with crushing force on the sharp edge of the dash. Wounds were sutured by Dr. Richard E. Straith with subcuticular stitches (after removing emergency interrupted sutures shown in first photograph). Crushed nasal bones were supported by my special splint, which was fixed to a head cast.

tained by contact with dashboard projections (fig. 6).

Type 3.—Infants and children are often injured and occasionally killed by crushing impact of skulls or faces on the dash. Teeth are frequently knocked out and faces cut on projecting knobs, cranks, "drop open" ash trays, etc. In more severe impacts the nose is frequently crushed; the malar and the upper jaw are frequently fractured, leaving pronounced facial deformities (figs. 7, 8 and 9).

Fig. 6.—Children are in the most dangerous position in the car when riding on mother's knee or standing up in front. Frequently childrens' teeth are broken off by hitting the dash in sudden stops, as happened to this child. The adult suffered a type 2 accident, her mouth coming down on a radio knob on the dash. Such projections should be eliminated and the dash should be crash padded to avoid such injuries.

Figure 9 shows the rather typical result of an accident. Note the slight steering post injury sustained by the driver (cut on chin) whereas the guest passenger received a crushing injury due to her impact on the dashboard.

Enforcement, Education and Engineering

For years traffic engineers have been talking about "engineering" with the three "E's": enforcement, education and engineering. To reduce this staggering toll of accidents and deaths, there must be cooperation in these phases.

Enforcement.—There must be enforcement of speed and other necessary traffic regulations. In all traffic surveys, speed is still rated as the greatest cause of accidents.

Education.—Since the age group from 18 to 24 produces the greatest number of accidents, education of youths at high school age is of paramount importance. Boys especially should be shown that, as drivers, they are in the safest seat in the car! What poor sportsmanship it is to drive recklessly and endanger the lives and faces of young girls who are usually the unlucky "guest passenger" victims!

There is no doubt, from the records of the patients at the Straith Clinic, that drinking was responsible for many accidents. Even distillers themselves advise every one to abstain from drinking for at least two hours before driving. If this rule were followed fewer accidents would result.

Fig. 7.—Type 3 injury left the impression of this woman's upper teeth in the instrument panel. At one point (arrow) a tooth actually penetrated the steel dash. The facial bones were crushed almost to pulp. Note deformity resulting as shown in figure 8.

Mothers should know that babies held on their knees occupy the most dangerous place in the car. They should hold children firmly if riding in the front seat or place them

Fig. 8.—Practically all the facial bones were fractured due to the impact on the dash as shown in figure 7. In spite of all efforts to maintain the fragment in position, this deformity resulted.

in proper carriers. Children should be kept from standing in the front (if possible, though I am well aware of the difficulty in doing this).

Engineering.—For the protection of the drivers, collapsible steering posts have been advocated. The horn rim could be placed on the underside of the wheel to prevent injury to face or chest in case of breakage. Raising and padding the lower edge of the dash would lessen knee injuries, and fewer floor pedals might minimize ankle injuries.

Since it is obvious that "guest passengers" are in the most dangerous position in automobiles, more attention should be paid to safety features in this part of the car.

Fig. 9.—These patients were forced off the road by an oncoming drunken driver. Though they had almost stopped, they hit a parked car. Note the typical slight chin injury sustained by the driver ("steering post injury") and the crushing "guest passenger" injury sustained by his wife, whose face struck the dash.

I have advocated[2] the removal of all knobs, cranks, drop down ash receivers, sharp ledges, etc., from the dash and the incorporation of rubber crash padding in front of the guest passenger. (Elimination also of sharp

Fig. 10.—This is the latest model of my crash pad which I have used for years on my cars. It can be adapted to any car, is hinged at the top for easy access to the glove box and offers adults and children much protection.

ash receivers and heavy robe rails and other attachments from the back of the front seat and provision of padding for the back edge of the front seat would minimize injuries to passengers in the back seat, who are frequently thrown forward.)

Hinging the windshield so that it would be forced outward by a force just short of the glass breaking point has been suggested. This would substitute the danger of a passenger's going through the opening and is therefore of questionable value.

For many years I have used, in my cars, a detachable crash pad to cover the dash in front of the guest passenger. If such a device were in common use, or crash padding

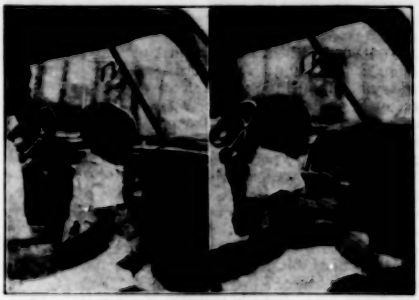

Fig. 11.—Babies on mothers' knees are in the most dangerous place in the car. Many have been killed by sudden stops, crushing their heads on the dash. The second photograph demonstrates the protection which children and adults should have when the crash pad is covering the dash.

incorporated in the dashboard, the facial injuries described would be reduced immensely (fig. 10). Children could ride in the front seat with less danger and with infinitely less anxiety on the part of the parents (fig. 11). Fortunately some car manufacturers are becoming more aware of these dangers to the guest passenger and are eliminating dangerous projections from the dash. Some are at long last adding crash padding to the instrument panel. It is hoped that others will follow suit to help reduce the staggering toll of accident victims.

2. Straith, C.L.: The Treatment of Facial Wounds Due to Motor Accidents, J. Michigan M. Soc., 34:64 (Feb.) 1935; Facial Bone Injuries, Dent. Digest (Oct.) 1933; Management of Facial Injuries caused by Motor Accidents, J.A.M.A. 108: 101 (Jan. 9) 1937; Automobile Injuries, J.A.M.A. 109:940 (Sept. 18) 1937; The Treatment of Crushing Facial Injuries, Proc. Inter-State Post-Grad. M. Assemb. North America, pp. 292-294, 1943.

Pneumonic Plague.—Rangoon has been "infected" off and on for the last quarter of a century, the reservoirs being rats and bandicoots. The pneumonic form, however, is rare. When recaptured in May, 1945, Rangoon was a severely devastated city and rehabitation proceeded slowly... Optimal conditions existed for the multiplication of rodents, and experienced observers were of the opinion that rats and bandicoots had never been so prevalent. Plague infection was confirmed among both species in 1945, but no sign of an epizootic was found. Human cases of bubonic plague in the city numbered 151 between May, 1945, and mid-August, 1946. The city was free from infection from the middle of August until late September, 1946. The village where the present outbreak began had shared in the bubonic epidemic in the spring, 17 cases being reported up to early April. Since that time the village also had been free from the infection. Pneumonic plague was not suspected until 10 persons had died, largely because the health authorities did not know the facts until a late date. The initial focus was the compound of a small soap factory in a village on the fringe of the city.—Wynne-Griffith, G., Pneumonic Plague in Rangoon, *Lancet*, April 24, 1948.

TULAREMIA IN THE OZARKS REGION

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In 1944 Heilman[1] demonstrated the sensitivity of Pasteurella tularensis to streptomycin under experimental conditions, and fifteen months later its clinical use in tularemia was reported by Foshay and Pasternack,[2] who noted the rapid regression of symptoms in 7 patients with ulceroglandular tularemia. Pulaski and Amspacher[3] reported successful treatment with streptomycin in 10 cases which occurred in United States Army hospitals, and Hunt[4] reported 12 cases of pleuropulmonary involvement in which streptomycin therapy was used, with prompt recovery in all except 1 case, in which death was attributed to pulmonary embolus. Seven cases of laboratory-acquired infection, successfully treated by streptomycin, were presented by Howe.[5] The National Research Council reported the treatment of 67 patients with 63 recoveries.

Before streptomycin became available, 27 patients with tularemia were seen at this hospital, and subsequently 27 patients have been treated with streptomycin. The purpose of this paper is to summarize the outstanding features of these 54 cases.

EPIDEMIOLOGY

The incidence of tularemia in this Ozarks region is increasing. In the interval from 1936 to 1940, 7 cases were recorded. From 1941 to 1944, 9 cases were seen and from 1945 to date 38 cases have been treated. Twenty cases have been seen thus far this year. Forty-one of the patients came from Northwest Arkansas and 13 from Southwest Missouri.

There was a definite seasonal incidence among these cases. Cases occurred during every month of the year; however, contrary to the observations of some authorities, 55 per cent occurred during May, June and July.

In contrast with statements concerning the most usual sources of the disease and the mode of transmission, it has been observed here that the source of the disease in 63 per cent of these cases was tick bites; in 14 per cent it was contact with rabbits, and in 4 per cent contact with squirrels. One patient gave a history of sticking a thorn in his finger at the site where the primary ulcer developed subsequently. The source of infection in 18 per cent of the cases was unknown. It was interesting to note that in each instance in which contact with an animal was considered the source of the infection, the patient gave a history of having had an abrasion at the site of the primary lesion previous to contact with the animal.

The incubation period, when it could be determined, varied from one to twelve days; however, 62 per cent were from one to three days. Five patients found ticks on their bodies at the site of the ulcer on the day of onset of symptoms. One unusual case presented an ulcer on the glans penis, hidden by the prepuce, with a tick imbedded in the center of the ulcer crater, of which the patient was unaware.

SYMPTOMS

The symptoms most commonly observed were malaise, chills, fever, generalized aching, anorexia, headache, sometimes nausea and vomiting and occasionally delirium. Rarely a rash of variable type appeared. The maximum temperature varied from 100 to 105 F., the average being 103 F. In most cases it remained more or less continually at a high level until the proper therapy was instituted. In some cases it exhibited regular remissions as seen in brucellosis. The pulse rate was usually proportional to the fever. The sedimentation rate was elevated, and in most cases there was leukocytosis. The white blood cell count ranged from 5,000 to 20,000, the average being 12,000. The differential white blood cell count was usually normal, but sometimes showed an increase in polymorphonuclear leukocytes. The spleen was sometimes enlarged.

Fig. 1.—Severe bilateral tularemic pneumonia with fatal outcome.

The site of the tick bite or contact with the animal was most commonly on the extremities with regional adenitis, with the lesions occurring as frequently on the lower extremities as on the upper. Ulcers did occur on the scalp, chest, abdomen, in the axillas and frequently on the penis or scrotum. In half of the cases with ulcers of the upper extremities epitrochlear adenitis developed. The unusually high frequency of the ulceroglandular pathologic changes occurring in the lower extremities, genitalia and abdomen (50 per cent) was undoubtedly due to the fact that ticks frequently attach themselves to the lower portions of the body.

Types of Tularemia

	Number of Cases	Percentage
Ulceroglandular	37	70
Pneumonitis alone	9	17
Typhoidal	1	0.5
Glandular	3	5.5
Oculoglandular	2	3.5
Ulcer alone	2	3.5
Total with pneumonitis	16	30

The cases of ulceroglandular and oculoglandular disease were nearly always correctly diagnosed promptly. In many cases, even before the reaction to the agglutination test was reported positive, the diagnosis had been made and the therapy started. However, the diagnosis

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1. Heilman, F. R.: Streptomycin in the Treatment of Experimental Tularemia, Proc. Staff Meet., Mayo Clin. **19**:553, 1944.
2. Foshay, L., and Pasternack, A. B.: Streptomycin Treatment of Tularemia, J. A. M. A. **130**:393 (Feb. 16) 1946.
3. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy of Tularemia in U. S. Army Hospitals, Am. J. M. Sc. **214**:144, 1947.
4. Hunt, J. S.: Pleuropulmonary Tularemia, Ann. Int. Med. **26**:263, 1947.
5. Howe, C., and others: Streptomycin Treatment in Tularemia, J. A. M. A. **132**:195 (Sept. 28) 1946.

in the cases of other types of the disease, particularly the pneumonic and typhoidal forms, was frequently delayed until therapeutic measures (e. g. penicillin for the cases of pneumonic disease) had failed and agglutination tests were done.

CASE 1.—The patient, a farmer aged 21 years, was admitted to the hospital in an acutely ill condition, complaining of pain and swelling of the left eye and eyelid. A few days prior to admission he had experienced general malaise, and twenty-four

Fig. 2.—Tularemic pneumonia; rapid recovery occurred under streptomycin therapy.

hours later the left eyelid and periorbital region began to swell, associated with fever. He had found several ticks on his body a few days prior to the illness, but he did not recall having been bitten, and was not in contact with animals. He was not aware of having had a foreign body in the eye.

Physical examination disclosed an acutely ill patient with a swollen and diffusely red left upper eyelid. The conjunctival surface of the lid exhibited a yellowish adherent membrane; the conjunctiva was red and edematous and the eyeball itself showed superficial injection. The fundus was not visible because of vitreous opacity. The right eye appeared normal. There was moderate edema of the left lower part of the face and upper part of the neck with pronounced cervical adenopathy. The temperature was 103 F. and the pulse rate 80. The white blood cell count was 7,100, with 70 per cent neutrophils and frequent smears and cultures of the eye were negative. A roentgenogram of the chest was normal, as was the urine. Because of suspected diphtheria, the patient received diphtheria antitoxin, which proved of no value, and his temperature ranged in a daily peak from 102 F. to 104 F. Six days after admission the agglutination reaction for tularemia occurred in a dilution of 1:80, and one week later it occurred in a dilution of 1:1,280. He was started on 0.4 Gm. of streptomycin every four hours, and the temperature immediately fell to normal, where it remained. The ocular symptoms subsided dramatically, but several cervical nodes became fluctuant, requiring surgical drainage. The streptomycin was continued until a total of 14 Gm. had been given. Recovery has been complete.

DIAGNOSIS

The definite diagnosis of tularemia depends on the agglutination tests. In many cases the serologic reaction was positive in high dilutions on the first examination. Any definite agglutination, even in the lowest titers, is significant; however, a positive diagnosis depended on a high or a rising titer. The highest titer among these cases was 1 to 42,240. Cross agglutinations in low dilutions with Brucella antigens were sometimes observed. It is commonly believed that the agglutination reaction becomes positive in the second week of the disease, but it was noted here that this interval varied widely. The interval ranged from eight to forty-three days, the average being fourteen days. In one fifth of these cases the agglutination reaction did not become positive before three weeks. Streptomycin did not appear to inhibit the development of specific antibodies.

TREATMENT

In April 1946 streptomycin became available for use at this hospital under the supervision of the National Research Council.

The course and prognosis of tularemia has been greatly affected by streptomycin. Prior to April 1946, 27 cases of tularemia had been observed, and since that time streptomycin has been used in 27 cases. Previous to this form of therapy, the morbidity after admission to the hospital varied from five to forty-five days, the average febrile period being fourteen days. Treatment varied, but in some cases included serum therapy and intravenous administration of bismuth sodium tartrate in addition to supportive care. In these 27 cases the mortality rate was 11 per cent. Twenty-two per cent of the patients had pneumonia, half of whom died. In addition to this long morbidity and high mortality convalescence required months, and relapses were common.

When streptomycin was used the morbidity dropped to an average of one day; with a maximum of six days. In most cases when a therapeutic blood level was attained, fever and other symptoms subsided dramatically. One patient was extremely ill and irrational on admission, and a history could not be obtained. Within twenty-four hours after treatment with streptomycin was started he had improved so dramatically that his only remaining complaint was weakness.

Of the 27 patients treated with streptomycin, 10 had pneumonia, and there were no deaths. In a few of these cases streptomycin was started before the agglutination test became positive in result. It is important to realize that the course of the illness may be far advanced before the agglutination becomes positive. Thus in cases of atypical pneumonitis in this region, in which a tularemic etiology is suspected, the use of streptomycin may be justified in face of a negative agglutination reaction, particularly when other antibiotics have failed.

CASE 2.—A white farmer aged 28 years was in good health when he cleaned a rabbit, seven days before he entered the hospital. At that time he had a small abrasion on his left index finger. Two days later he noted pain, swelling and purulent drainage about the abrasion, associated with swelling and tenderness of the epitrochlear and axillary lymph nodes. When seen by his family physician he had a temperature of 103 F. and had vomited several times. The physician administered sulfonamide compounds and salicylates; however, the symptoms continued until admission here.

Examination revealed an acutely ill, febrile patient. His temperature was 101 F., his pulse rate 90 and his respiration rate 24. The skin was hot and dry. There was a small tender, crusted abrasion on the dorsum of the left finger which was swollen and inflamed. There were several large, soft, tender epitrochlear and axillary lymph nodes on the left side which were freely movable. The heart, lungs and abdomen were normal.

The initial impression was tularemia of the ulceroglandular type. The patient's temperature rose to 103 F. A roentgenogram of the chest was normal, and on the day after entry the agglutination test for tularemia was negative in reaction. Two days later the reaction was still negative; the patient was started on specific therapy and within twenty-four hours his temperature had declined to 99 F.; it remained below this level thereafter. On the sixth day the agglutination reaction was

still negative, but on the following day (i. e., fourteen days from the onset of symptoms) it became positive in a dilution of 1:10. Six days later it became positive in a dilution of 1:1,280. The patient had recovered long before and was discharged cured.

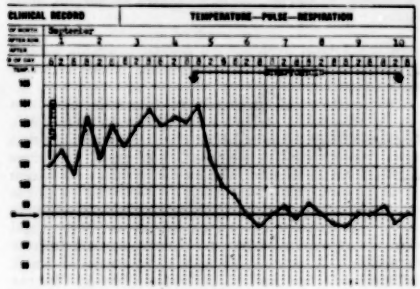

Fig. 3.—Temperature graph illustrating rapid response to streptomycin in a case of severe ulceroglandular tularemia.

Because the optimum dosage of streptomycin had not been established, dosages were varied according to the type and severity of the disease and the patients' response to therapy. The most common schedule was 1.0 to 1.25 Gm. daily in divided doses every three or four hours. A few cases, in which the desired response was not obtained on this program, exhibited prompt resolution of symptoms when medication was increased. Total dosage in cases of ulceroglandular disease varied from 3.75 to 14 Gm., the average being 7 Gm. Three patients received only 5 Gm. with good results. In the pneumonic forms the average dose was also 7 Gm., with a range of 5 to 14 Gm. Likewise, 3 patients with pneumonia were treated satisfactorily with 5 Gm. of the drug. Results obtained from the various dosage schedules were all essentially the same; i. e., excellent.

The resolution of the pneumonic process is slow regardless of treatment with streptomycin. This drug stopped the extension of the pulmonary pathologic changes, but the process of resolution usually required two to three weeks, and occasionally a residual fibrosis remained indefinitely.

Healing of the tularemic ulcer begins soon after treatment with streptomycin is started and is usually complete within one week. In some cases there was a secondary infection which responded to moist dressings. In most of the cases the affected regional lymph nodes healed slowly, but not infrequently they became fluctuant, and if not incised would, many times, remain abnormal for several weeks, rupturing spontaneously. It was found that surgical drainage reduced the healing interval considerably.

SUMMARY

An analysis of 54 cases of tularemia is presented. The incidence of the disease appears to be increasing in this Ozark region. The majority of the cases occurred during the summer months. In 63 per cent of the cases the source of the infection was tick bites.

The incubation period varied from one to twelve days but averaged one to three days. The symptoms in these cases did not vary significantly from the usual description. One or more cases of each type of the disease were seen, with 70 per cent representing the ulceroglandular form. Seventeen per cent of the patients had pneumonic involvement.

The definite diagnosis of tularemia depends on a positive agglutination reaction in either a high or a rising titer. The interval from onset of symptoms to the development of specific agglutinations ranged widely from eight to thirty-three days, with an average of fourteen days.

Twenty-seven cases in which treatment was with streptomycin were compared with an equal number of cases in which treatment was only symptomatic. An average morbidity of fourteen days and a mortality of 14 per cent were noted in the latter group, in contrast with an average morbidity of one day and no mortality in the cases in which treatment was with streptomycin. Previous to the use of streptomycin 50 per cent of the cases of pneumonic disease were fatal.

The indications for the use of streptomycin do not necessarily include a positive agglutination reaction, because the course of the illness may be far advanced before this test elicits a positive reaction. Thus, in this region, the ulceroglandular syndrome with fever is in itself an indication for immediate specific therapy.

The most common dosage schedule was 1 to 1.25 Gm. of streptomycin daily in divided doses every three or four hours, the total usually amounting to 5 to 7 Gm. It was noted that the average case of pneumonic disease required little, if any, more streptomycin than the cases of ulceroglandular disease.

PERMANENT WAVE PROCESS

Clinical Report With Special Reference to the Effect of Ammonium Thioglycolate on the Skin

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and WILLIAM McDANIEL, M. D.
Cincinnati

It has been estimated by manufacturers of chemicals employed in permanent hair-waving procedures that some "permanent wave process will be carried out at least fifty million times during the current year."[1] There is then, an apparent need for a critical study of the irritant properties of the chemicals so casually applied to the hair and scalp.

Permanent hair-waving methods are classified by Reed, Humoller and DenBeste[1] into two main categories. Briefly, in the "hot method, the hair is treated with an alkaline sulphide preparation and wrapped around a rod of small diameter. Heat is then applied to change the configuration of the hair from a straight to a curled state." In the "cold method, the hair is also wrapped around a rod of suitable diameter either prior to or after treatment with an alkaline reducing agent—usually thioglycolate. In contra-distinction to the hot permanent waving method, no external heat is applied. After satisfactory undulation of the hair is obtained, the wave is fixed by application of a suitable oxidizing agent."[1]

The mechanism of the latter waving reaction and the supposed changes in the chemistry and structure of the hair under these circumstances provide an interesting example of the application of biochemistry in dermatology. However, clinical interest at present derives chiefly from the possibilities for injury to the hair and the scalp which may accompany the procedures of cold waving. Many clinical and experimental reports have appeared in the literature, and some of these

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1. Reed, R. E.; Humoller, F. L., and DenBeste, M.: Permanent Waving of Human Hair: The Cold Process, read before the meeting of the American Association for the Advancement of Science (December) 1946.

have been confusing and contradictory. This situation illustrates once more a principle that all too frequently is neglected, that the potentialities for harm possessed by commercial products should be fully investigated before they are distributed and used. Rattner [2] has indicated that there have been only about twenty-two complaints among 50,000 treatments.

Cotter [3] reported 5 cases of dermatitis associated with the application of cold waving processes. Patch tests were carried out on 2 of these persons, but the details of the concentrations of the materials employed were not given. McCord [4] has reported that certain commercial preparations of ammonium thioglycolate caused injury to the skin of 7.4 per cent of persons subjected to contact therewith for twenty-four hours, but no injury resulted from similar contact for four, six or nine hour periods. McCord [4] is also authority for the statement that no primary irritation of the skin occurs as the result of contact with thioglycolic acid or its alkaline derivatives in concentration (in water) below 8 per cent by volume. Moreover, McCord [5] found no evidence of sensitivity or allergic response of the skin to carefully prepared ammonium thioglycolate. According to Cappel and Cappel,[6] the incidence of injurious effects, in the wake of thirty million or more cold waves that have been given within three years, has been under 0.1 per cent. These investigators applied cotton saturated with the material to the skin and covered it with a watch glass, the edges of which were sealed on the skin with collodion. Goodman [7] claimed that the patch test is not reliable for the detection of dermatitis from cold wave preparations, since the factor responsible for the irritation is usually a combination of thioglycolic acid, the softener, the fixative or the keratin, rather than the thioglycolic acid itself. Howell [8] reported a case of eczematous contact dermatitis following the application of a cold waving process. No positive reaction was observed when waving solution, neutralizing liquid and shampoo were employed individually in patch tests. He also carried out patch tests, with negative results, on 3 normal persons with 1 per cent concentrations of the shampoo, preliminary lotion, waving compound and neutralizing solution, and mixtures of these chemicals. When the patient was tested with the preliminary lotion, one month after the dermatitis subsided, a positive reaction was elicited in twenty-four hours. This preliminary lotion was a special type of detergent of unknown composition, used to cleanse the hair. McGill and Rag [9] wrote that 11 cases had been reported to the Division of Industrial Hygiene in Oregon and that none of the diagnoses had been confirmed. One patient had failed to respond positively to a patch test with the cold waving solution diluted with 100 parts of water. In a second case reported by these authors patch tests were not made.

In addition to the possibility of cutaneous irritation and sensitization from thioglycolate, there are, of course, some definite effects on the hair. The changes include drying, splitting, changes in tensile strength, elasticity and, of course, cellular state. Clinically, these changes may be manifested by changes in the color of the hair; for example some darkening of white hair; and by splitting, cracking and desiccation of the hair. It does not matter how correct or "mild" the permanent waving process may be, there still are a number of changes in the hair, which, for this reason, is not in a normal state after the cold waving process.

Systemic toxicity from cold waving must also be considered. Cotter [3] has suggested this in his report, but he gives no evidence of its occurrence. Some detailed observations have been made on animals in this regard. According to Whitesell, Alvarez and Draize,[10] salts of thioglycolic acid may be absorbed percutaneously by animals with resultant systemic poisoning, "but the dose level is higher and the manner of application more vigorous than those specified in directions accompanying waving solutions intended for use by beauticians and in home application." There were minor fluctuations in the hemoglobin content of the blood and in the volume of erythrocytes of animals following dosages as small as 4 cc. per kilogram per day. In general, however, the conclusion arrived at from these studies was that ammonium thioglycolate hair-waving solutions are "safe" for use if the usual directions are carefully followed. Rostenberg,[11] who has had considerable experience with the analysis of reports of irritations from consumer products, expressed the belief that many prefer the cold wave to the discomforts incident to their use.

Since the cold wave process as practiced in the beauty parlor is an elaborate ritual, which involves the application of many things in addition to the thioglycolate solution, the correct analysis of any irritation presumed to have followed use of the cold waving process demands multiple cutaneous testing with all the ingredients used in the various steps of the cold waving process. These should include: (1) the preliminary shampoo material, (2) the preliminary cleansing lotion, (3) the cold wave material, (4) the oxidizing agent, (5) the post-treatment shampoo material, (6) the wave setting material, perfumes, etc.

EXPERIMENTAL OBSERVATIONS

Preliminary observations have been made to determine the effect of the application of undiluted and diluted ammonium thioglycolate on the normal scalp and the normal skin of women. For this purpose 149 women patients with apparently normal skin and scalp were employed as subjects. Thirty of these were Negro. Small quantities of the undiluted ammonium thioglycolate were sealed by means of paraffin into a series of small bottles for use as required. In an effort to approximate the conditions under which the cold waving procedure is carried out, 1 drop of the undiluted ammonium thioglycolate solution was applied by means of a glass rod and rubbed into the occiput, while another drop was rubbed into the clear skin of the forehead just below the hair line, this procedure being designated as a "streaking technic." On the same occasion, in many instances, a conventional contact patch test of the undiluted material was made, the observations on these being concluded in forty-eight hours.

The results of the unstandardized "streaking tests" were disappointing, even though an occasional positive

2. Rattner, H.: Personal communication to the authors.
3. Cotter, L. H.: Thioglycolic Acid Poisoning in Connection with the "Cold Wave" Process, J. A. M. A. 131:392 (June 15) 1946. Effects of the Cold Wave Process, editorial, ibid. 131:746 (June 29) 1946.
4. McCord, C. P.: Toxicity of Thioglycolic Acid Using Cold Wave Permanent Process, J. A. M. A. 131:776 (June 29) 1946.
5. McCord, C. P.: The Physiologic Properties of Thioglycolic Acid, Indust. Med. 15:669 (Dec.) 1946.
6. Cappel, N. A., and Cappel, L. H.: Cold Permanent Wave Solutions as an Irritant, Am. Perfumer & Essential Oil Rev. 48:143 (Aug.) 1946.
7. Goodman, H.: Dermatitis from Cold Wave Permanent Chemicals, Urol. & Cutan. Rev. 49:117 (Feb.) 1945.
8. Howell, J. B.: Contact Dermatitis from Cold Permanent Waving, Arch. Dermat. & Syph. 49:432 (June) 1944.
9. McGill, C. M., and Rag, L.: Cold Wave Dermatitis: Report of Two Cases, Indust. Med. 16:238 (May) 1947.
10. Whitesell, M. F.; Alvarez, E., and Draize, J. H.: The Percutaneous Toxicity of Thioglycolates, Federation Proc. 6:383 (March) 1947.
11. Rostenberg, A., Jr.: Personal communication to the authors.

reaction was obtained. There was no correlation between such reactions and the positive reactions to the patch tests. Conversely, the subjects with the positive reactions to patch tests gave negative reactions to "streaking tests." It is believed however, that if the "streaking test" could be standardized as regards pressure, temperature and the duration of actual contact with the skin, information concerning the applicability of the test of the properties of chemical substances could be obtained.

TABLE 1.—*The Results of the Application of Ammonium Thioglycolate Solution to the Skin of Human Subjects by a "Streaking Technic"*

Material Tested	Number of Subjects	Reactions: Negative	+	++	+++	Positive ++++
Undiluted ammonium thioglycolate, scalp	83	81	0	2	0	0
Undiluted ammonium thioglycolate, forehead	83	83	0	0	0	0

The eleven reactions obtained in routine forty-eight hour patch tests carried out on 83 patients suggest that this compound is a mild irritant for the skin when applied in undiluted form over a prolonged period of time.

Twelve beauty parlor operators with contact dermatitis of the hands were examined. In general, the majority of these cases showed the irritant type of contact dermatitis, with solitary, thickened, fissured and occasionally vesicular, oozing patches. It is important, that in no case was a positive reaction produced to a patch test with the cold wave material which the beauty parlor operators furnished. Tests with the shampoos

TABLE 2.—*Results of Application of Ammonium Thioglycolate Alone and After Admixture with Soap Solution to Scalp and Skin of Human Subjects by a "Streaking Technic"*

Material Tested	Number of Subjects	Reactions: Negative	+	++	+++	Positive ++++
Undiluted ammonium thioglycolate, scalp	63	61	2	0	0	0
1% soap solution, scalp	63	62	1	0	0	0
Undiluted ammonium thioglycolate plus 1% soap solution, scalp	63	62	1	0	0	0
Undiluted ammonium thioglycolate, forehead	63	63	0	0	0	0
1% soap solution, forehead	63	63	0	0	0	0
Undiluted ammonium thioglycolate plus 1% soap solution, forehead	63	63	0	0	0	0

gave positive reactions with much greater frequency. This observation substantiates a clinical impression that the majority of cases of dermatitis related to cold waving materials are characterized by direct irritation or even nonallergic eczematous dermatitis (Baer) and not sensitization. In view of the prolonged periods of contact associated with friction which the beauty parlor operator has with these solutions, it is strange that not more of these reactions are produced. In cold waving done in the home, where 1 person does the hair of a number of subjects, the hands of the operator may also become irritated.

Five patients with dermatitis presumed to have followed cold waving of the hair were studied. In 1 instance, the cutaneous reaction followed the use of a "hot" waving solution. In no case was an extensive eczematous type of reaction produced. The clinical forms of dermatitis which may follow the cold waving process may be divided roughly into three classes: (1) a pruritic, discreet, papulopustular and vesicular eruption scattered over the back of the scalp, about the ears and about the shoulders; (2) the solitary deep burn type of lesion (more common in "hot" waving?). If this is deep enough alopecia may result; (3) rarely, an eczematous contact dermatitis of the hair line and occasionally of the scalp.

No effort was made to gather the details of the performance of the operators of the cold waving processes carried out on these patients, with regard to carelessness, expertness, precautionary measures and the period of

TABLE 3.—*Results of the Application of Ammonium Thioglycolate to the Skin of Human Subjects by the Patch Test Technic*

Material tested	Number of Subjects	Reactions: Negative	+	++	+++	Positive ++++
Undiluted ammonium thioglycolate	83	72	8	2	1	0

contact permitted. The shampoo was implicated most frequently by the patch tests, and in some instances no positive reactions to any of the substances were obtained. There is definite need for a critical study of the irritation of the skin of the beauty parlor operators who work with cold waving solutions, and also of patrons of beauty parlors who complain of various degrees of cutaneous irritation following the use of cold waving solutions. It is our impression from clinical observation that irritation of the skin, while uncommon, is yet more frequent in its occurrence in this relationship than is eczematous dermatitis. Considering the strength of the solutions employed in cold waving process, it is indeed surprising that more cases of cutaneous irritation do not result.

COMMENT

From preliminary observations, then, it is evident that the technic of cold waving can produce local irritation of the skin. Some persons appear to be more susceptible to this irritation than others. Some factors which may be considered are the differences in the materials employed and the technics of their use. These factors have not been determined in a critical fashion. Rarely, eczematous hypersensitivity may be produced in the cold waving process. It seems that this eczematous hypersensitivity is more frequently due to materials other than the cold waving solutions themselves and, as Peck and Schwartz [12] mentioned, especially the perfumes, gums and resins. Preliminary use of thioglycolate in the foregoing series of cutaneous tests has demonstrated that it is, potentially, a mild irritant for the skin.

These few facts suggest that it may be possible to develop some prophylaxis of irritation from thioglycolate. When the material is used with considerable caution, there may yet be some dermatitis about the neck from the seepage of ammonium thioglycolate between towels and the surface of the neck and from the rubbing of this into the skin. Similarly, the dermatitis of the scalp may be due to unduly prolonged contact of the ammonium thioglycolate with the scalp, to inadequate removal of the material after its effect has been achieved or to its incomplete neutralization at the proper time.

However, the chief difficulty in the use of ammonium thioglycolate in relation to cutaneous damage lies in its effects on beauty parlor operators rather than on the patrons. The specific background of such irritation can rarely be proved by the diagnostic procedures available at present, since the lesions are nonspecific, being those of primary irritation. From a practical standpoint, it is

12. Schwartz, L. B., and Peck, S. M.: Cosmetics and Dermatitis, New York, Paul B. Hoeber, Inc., 1946, p. 103.

V 1
194

not possible to protect the skin of beauty parlor operators during their performance of cold waving technic, since the technic is an open and wet one, and the hands, especially the left, are dampened continuously by repeated applications of the solution. In addition, the frequent use of detergents associated with the process would appear to be a contributory factor. Beauty parlor operators refuse to use gloves, and the process at present does not appear to be amenable to control from the aspect of complete avoidance of contact on the part of the operators.

The following recommendations are offered for the purposes of prophylaxis:

1. Attempts to prevent irritation from ammonium thioglycolate: The beauty operator should be instructed emphatically that no matter how rapidly she works and no matter how anxious she is to complete her work no large quantities of the cold waving materials should be allowed to remain on the surface of the skin, and that as far as possible none should be permitted to remain longer than is required to remove it from such skin surfaces as those of the neck and forehead, which are not covered with hair.

2. Ammonium thioglycolate adjacent to a scratch, or to an area which has been rubbed by towels or abraded by other manipulations of curling equipment or other appliances, may also serve to induce an actual dermatitis. Thorough rinsing of the scalp is recommended to prevent this so far as possible.

3. The operator should pay close attention to any complaints of burning and discomfort which the patient exhibits. Areas so involved can be and should be cleansed as completely as possible by mopping up the excess which has accumulated thereon.

4. Following the appearance of actual erythema or redness of the scalp or of the neck, further contact with the permanent waving solution should be avoided, since further contacts will certainly cause an increase in the irritation.

5. Towels and towel rests should be inspected from time to time to see whether any of the cold waving solutions have been allowed to drip or remain on them.

6. During the operation of cold waving, every attempt should be made to limit the use of materials to the least quantities consistent with obtaining the effect and to avoid spillage and undue spread of the materials.

7. The beauty parlor operator should attempt to protect her hands as much as possible during the cold waving operations: (*a*) by attempting to use materials and appliances which do not allow repeated contacts with her hands; (*b*) by avoiding undue dependence on the so-called protective cream; (*c*) by using protective gloves when necessary, especially if the skin of the hands should be irritated or abraded, and (*d*) by avoiding all contact with cold waving preparations or strong detergents for a "significant" period of time when the skin of the hand is irritated or thickened.

When actual dermatitis is found to have occurred in close or plausible time relationship to contact with cold waving materials, an effort should be made to classify the type of dermatitis. This is to say, one must decide whether the dermatitis is a discreet, localized irritation of the scalp and skin, what the degree of this irritation is and whether or not it is an eczematous type of contact hypersensitivity. Next, the patient should be tested carefully and adequately with all the materials that have been used in the entire technic of the cold waving process. As the result of the collection of such data on a sufficient number of cases, the true picture can be found and proper corrective measures outlined.

SUMMARY AND CONCLUSION

Cold waving solutions are used extensively, and the frequency of reactions is reported to be less than 0.1 per cent. The reactions may be characterized either as varying degrees of primary irritation or, more rarely, as instances of eczematous hypersensitivity. The reactions on the hands of the beauty parlor operators are more frequent by far, more severe and more extensive than those which occur among patrons of the beauty parlors.

In a preliminary group of observations on 149 women, ammonium thioglycolyate was found to be a mild irritant to the skin. Attempts were made to simulate actual practice by the use of "streaking tests" on the scalp and the forehead. There were a few reactions to this procedure, but these effects were not correlated with the response to a conventional forty-eight hour patch test.

Recommendations have been made for the avoidance of procedures on the part of the operators which would appear to increase the hazard of cutaneous irritation to patrons.

Little hope is held for the protection of the hands of the beauty parlor operators under the conditions associated with present procedures, unless they will consent to wear some sort of protective gloves.

VARIOUS PHASES OF THE USE OF STREPTOMYCIN IN TUBERCULOSIS

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Streptomycin, a recently developed antibiotic, figures prominently at the present time in the chemotherapy of tuberculosis in man. During the twentieth century the development of chemotherapy in tuberculosis in man has been pursued by two apparently divergent sets of investigators: first, those who believed in conservative progress based on thorough fundamental scientific study of possible therapeutic agents, translating elucidating laboratory and animal findings into human values; and second, those who were content to quickly transpose apparently encouraging in vitro and in vivo animal findings into human significance. The second group, of course, took encouragement from findings in diseases where only human studies were possible and from the fact that animal disease did not duplicate sufficiently that noted in man and therefore did not permit the latter to be interpreted in the light of such scientific knowledge. Yet it is odd that the second group frequently justify their failures, both in interpreting human results and in supporting their contentions, on the basis of the results of animal tests.

There are definite features of streptomycin which preclude an early and ready evaluation of its effects in human tuberculosis, a disease from which man recovers with only the aid of nature and good medical sense to live his allotted three score plus ten. The investigations to be reported here were undertaken with the sole purpose of building scientific information that would enable us to determine whether streptomycin and similar chemotherapeutic agents might be beneficial in tuberculosis in man and, further, to explain so far as possible its mode of action in man. Much has been written to date on streptomycin, and that part published previously to the middle of 1946 has been reviewed by us.[1]

It is claimed that "streptomycin exerts a suppressive effect on the progress of tuberculous infection in man.

From the Research Department, National Jewish Hospital.
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This study was aided by the Jacques Loberrore fund for tuberculosis research.

1. Corper, H. J., and Cohn, M. L.: The Tubercle Bacilli and Fundamental Chemotherapeutic and Antibiotic Action, Yale J. Biol. & Med. 19:1-22, 1946.

Limitations to the intensity of the antibacterial activity and possibly to its duration have been demonstrated."[2] In a report of the results of a study of 100 treated patients it is noted that "Streptomycin is an antibacterial agent which possesses the unique ability to inhibit the growth of Mycobacterium tuberculosis in vivo, both experimentally and clinically. . . . In many instances streptomycin appears to suppress tuberculosis rather than to eradicate it, being apparently tuberculostatic rather than completely bactericidal in the concentrations which can be obtained in the tissues. . . . consistently encouraging results attendant on its use in a series of 100 cases in the past two years" is claimed.[3] It is admitted, however, that a critical evaluation of the human study leaves much to be desired so far as definite results are concerned and that the standard accepted treatments of the past should not be forsaken. Aside from such general reports, there are individual case reports indicating a definite curative effect of streptomycin in human tuberculosis. One such, appearing as recently as March 1947 and reporting the successful treatment of 4 children (7 months to 3 years of age), who were given 1 Gm. daily for only one month, stated that this resulted "in defervescence in all 4, improvement in their general conditon and a regression of the appearance of the pulmonary lesions in the roentgenograms."[4] Such uncontrolled observations can only lead to a misconception of the actual value of streptomycin, if one exists, in man and the indiscriminate abuse of the treatment, without benefit.

In a previous publication we noted[1] that "streptomycin properly administered and in proper dosage is capable of retarding the development or growth of human tubercle bacilli, both in vitro and in vivo" in restricted laboratory experiments. "The concentration of streptomycin required to retard the growth of tubercle bacilli in vitro in good nutrient medium can only be attained in vivo for a brief period by any route of administration or amount of streptomycin that can be used even with the present high assay unit preparations. . . . There is no evidence available at present to indicate that streptomycin enters the important organs in appreciable amount for any significant time although it is present in the blood, or that it accumulates in these organs," or "that tubercle bacilli adsorb or absorb streptomycin or that it accumulates in these bacilli in vitro or in vivo."

Although their number is difficult to determine accurately, only few other reports on the organic distribution of streptomycin have appeared. Adcock and Hettig[5] studied the absorption, distribution and excretion of streptomycin in man. It was not absorbed appreciably when given orally or by inhalation, and a high concentration appeared in the feces after oral use. After parenteral administration, it was demonstrated in the blood serum in amounts roughly proportional to the dose, and appeared in the bile, the spinal fluid of subjects with meningitis, and in the pleural fluid in effusions. A postmortem study of its distribution, after it had been given by continuous subcutaneous infusion in excess of forty-eight hours extending to the time of death, revealed that it was present in high concentration in the kidney. Smaller amounts were found in the lung and in the heart muscle, while both the brain and the liver were virtually free from the substance. From 41 to 86 per cent of streptomycin was excreted in the urine within twelve hours after parenteral administration. More recently Nelson, Forgacs and Kucera[6] found no streptomycin in the organs of the mouse one hour after injecting 1,000 units. Using electronegatively charged trypan blue for anchoring the streptomycin, they were able to note it in determinable amounts in the blood, the liver and the spleen after twenty-five hours.

An earlier report by Zintel and co-workers[7] noted that after parenteral administration most of the streptomycin (29 to 89 per cent) is recovered from the urine in twenty-four hours, and little or no more is recovered after this. Streptomycin was found in most of the body fluids—blood, ascitic fluid, pleural fluid, aqueous humor, vitreous humor, amniotic fluid and bile. Small amounts were found in the spinal fluid, increasing in the presence of meningitis. Donovick and Rake,[8] using the mouse, recovered 61 per cent of the streptomycin from the urine with large doses and 45 per cent with smaller doses. Four hours after injection, 100 per cent of the drug was found.

That tubercle bacilli may acquire resistance to streptomycin, another feature of uncertain significance, is recorded. Its practical implication in regard to man is still unknown." Streptomycin-resistant human type tubercle bacilli were found to be as virulent for white mice as streptomycin-sensitive strains. Infection produced in mice with streptomycin-resistant cultures were not suppressed by streptomycin treatment. Middlebrook and Yegian[10] noted that in all mycobacteria thus far tested resistance to streptomycin developed in vitro at a rapid rate and that it persisted for at least four months and appeared not to be paralleled by any diminution of virulence for guinea pigs.

THE IN VITRO EFFECTS OF STREPTOMYCIN

In earlier studies we showed that streptomycin was perceptibly less effective in retarding the growth of human tubercle bacilli on a good nutrient medium (egg yolk) than on a poor nutrient medium (broth agar) and that the amount of planting played a significant role in its effect on the bacilli. In a further study with liquid mediums, usually graded as poor nutrients for tubercle bacilli, rather interesting findings were recorded, which emphasizes the necessity of accurately defining the conditions under which retardation of growth occurs in tubercle bacilli or acid-fast bacilli influenced by streptomycin. In a preliminary titration test with the acid-fast bacillus "Day," it was found that while this organism would not grow in a dilution of less than 0.01 mg. per cubic centimeter of fine

2. Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Streptomycin in the Treatment of Clinical Tuberculosis, Am. Rev. Tuberc. **54**: 191-201, 1946.

3. Hinshaw, H. C.; Feldman, W. H., and Pfuetze, K. H.: Treatment of Tuberculosis with Streptomycin: A Summary of Observations on One Hundred Cases, J. A. M. A. **132**: 778-782 (Nov. 30) 1946.

4. Sanford, H. N., and O'Brien, D. E.: Streptomycin in Pulmonary Tuberculosis in Childhood: Results in Four Children, J. A. M. A. **133**: 691-693 (March 8) 1947.

5. Adcock, J. D., and Hettig, R. A.: Absorption, Distribution and Excretion of Streptomycin, Arch. Int. Med. **77**: 179-195 (Feb.) 1946.

6. Nelson, W. E.; Forgacs, J., and Kucera, J. L.: Alteration of the Distribution and Excretion of Streptomycin, Proc. Soc. Exper. Biol. & Med. **64**: 20-21, 1947.

7. Zintel, H. A.; Flippin, H. F.; Nichols, A. C.; Wiley, M. M., and Rhoads, J. E.: Studies on Streptomycin in Man: I. Absorption, Distribution, Excretion and Toxicity, Am. J. M. Sc. **210**: 421-430, 1945.

8. Donovick, R., and Rake, G.: Studies on Some Biological Aspects of Dihydrostreptomycin, J. Bact. **53**: 205-211, 1947.

9. Youmans, G. P., and Williston, E. H.: Effect of Streptomycin on Experimental Infections Produced in Mice with Streptomycin Resistant Strains of M. Tuberculosis var. Hominis, Proc. Soc. Exper. Biol. & Med. **63**: 131-134, 1946. Karlson, A. G.; Feldman, W. H., and Hinshaw, H. C.: Persistence of Resistance of Tubercle Bacilli to Streptomycin During Passage Through Guinea Pigs, ibid. **64**: 4-7, 1947.

10. Middlebrook, G., and Yegian, D.: Certain Effects of Streptomycin on Mycobacteria in Vitro, Am. Rev. Tuberc. **54**: 553-555, 1946.

suspension planted in plain broth, the addition of 1 per cent dextrose to the medium altered this. In Wong Weinzirl's medium, a synthetic nonprotein medium without dextrose, growth occurred in 0.001 mg. per cubic centimeter plantings; and after the addition of 1 per cent dextrose, growth occurred in the 0.0001 mg. plantings, indicating the better growth-supporting nutrient qualities of the latter medium as compared with the former for acid-fast saprophytes as well as for tubercle bacilli. With the information at hand, the effect of streptomycin on standard plantings of acid-fast and tubercle bacilli was tested on a broth-unit basis with the results recorded in table 1. In addition, this table shows the effect of the addition of a non-nutrient, nontoxic, apparently inert soluble colloidal cellulose preparation.

Table 1.—*A Comparison of the Growths of Acid-Fast Saprophyte "Day" on Plain Broth and on Wong's Medium and in Wong's Cellulose Gum**

Streptomycin Broth "Day" Units per Cc. of Medium	Plain Broth	Broth with 5% Glycerin	Broth with 1% Dextrose	Wong's Medium with 5% Glycerin, 1% Dextrose	Wong's Cellulose Gum with 5% Glycerin, 1% Dextrose
500	0	0	0	0	0
50	0	0	0	0	0
10	0	0	0	0	+++
5	0	0	0	+	+++
2	0	0	+	++	+++
1	0	++	++	+++	+++
0.5	++	++	++	+++	+++
0.5	++	++	++	+++	+++

* The tubes were all planted with 1 mg. per cubic centimeter of the acid-fast "Day" bacilli, and readings were made after two days at 37 C. Essentially the same results were noted with tubercle bacilli in similar tests.

The results recorded in table 1 indicate that the amount of streptomycin required to retard the growth of acid-fast bacilli can vary in liquid mediums from 1 unit for plain broth to 5 units for broth with dextrose, to 10 units for a synthetic nonprotein medium (Wong's) containing glycerin and dextrose, to over 100 units for the latter containing an inert non-nutrient soluble colloidal cellulose substance, in spite of no apparent change in the hydrogen ion concentration of the medium or loss of activity of the contained streptomycin as tested at the end of the experiment on a broth-unit basis.

The latitude of the arbitrary retardation produced in vitro by streptomycin is again evident if the tests are performed on a poor nutrient medium, such as glycerin agar, which requires relatively heavy plantings of the bacilli if evident growth is to be obtained. The growth on such a streptomycin-containing medium, the Wong glycerin agar medium, and the effect of the development of resistance to the streptomycin are presented in table 2.

It is noted from the results recorded in table 2 that tubercle bacilli are capable of growing directly on 10 to 1,000 units of streptomycin per cubic centimeter contained in a relatively poor nutrient solid medium, such as Wong's glycerin agar without dextrose, and that a first transplant from cultures containing 50 units of streptomycin invariably grew on 1,000 to over 10,000 units of streptomycin per cubic centimeter. It must be remembered that there is a striking difference between the growth of tubercle bacilli on nutrient liquid mediums and that on the same constituents incorporated in agar mediums, as pointed out by us years ago and verified recently by Dubos. The agar mediums require much heavier plants for successful growth. Another feature complicating interpretation and measurement of in vitro streptomycin retardations of tubercle bacilli and acid-fast bacilli is the fact that the micro-organisms will not grow on serum, plasma or blood directly unless these have been diluted with a nutrient medium or subjected to some other denaturing influence, such as heating or prior acid treatment and neutralization.[11] On the other hand, they will grow on organs, but the streptomycin unitage is disturbed. These findings with tissues and body fluids are presented in table 3.

The results recorded in table 3 indicate that at least 5 to 10 units of streptomycin is required to inhibit growth of acid-fast bacilli in ground organs (lung, liver, spleen and kidney), and, in spite of the fact that citrated plasma and blood sediment (red corpuscles) completely retard the growth of acid-fast bacilli (and tubercle bacilli), from 10 to 100 units of streptomycin is required to produce a retardant effect when these body fluids are diluted with Wong's liquid medium. The natural retardant action of the plasma is destroyed by heating for thirty minutes above 50 C.

Previously it was demonstrated that streptomycin can be found in the blood after injection but not in the heated organs. In an attempt to determine whether streptomycin could be demonstrated by unit assay in the fresh organs of exsanguinated guinea pigs, several animals weighing about 700 Gm. were given 125,000 units of streptomycin. One hour after injection of the streptomycin the organs were removed aseptically and used undiluted and diluted up to 1:5 with solution of sodium chloride for implantation of acid-fast sapro-

Table 2.—*The Growths of Various Strains of Tubercle Bacilli and an Acid-Fast Saprophyte on a Synthetic Nonprotein Glycerin Agar Medium (Wong) Without Dextrose* Containing Different Concentrations of Streptomycin*

Strain of Bacilli Used	Growth with Given Concentration of Streptomycin (Broth "Day" Units per Cubic Centimeter) in Wong's Glycerin Agar Medium (Without Dextrose)																	
	0 Units		1 Unit		10 Units		50 Units			100 Units			1,000 Units			10,000 Units		
Avirulent human tubercle bacilli	+S†	+L	0S	+L	0S	+L	0S	+L†	+T	0S	+L	+T	0S	+L	+T	0S	+L	+T
Virulent human tubercle bacilli																		
No. 4038 ‡	+S	+L	+S	+L	0S	+L	0S	+L	+T	0S	+L	+T	0S	0L	+T	0S	0L	+T
H 168 ‡	+S	+L	+S	+L	0S	+L	0S	+L	+T	0S	+L	+T	0S	+L	+T	0S	0L	+T
Glucksom	+S	+L	0S	+L	0S	+L	0S	+L	+T	0S	+L	+T	0S	+L	+T	0S	+L	+T
H 37/rv ‡	+S	+L	0S	+L	0S	+L	0S	+L	+T	0S	+L	+T	0S	0L	+T	0S	0L	+T
Virulent bovine tubercle bacilli	+S	+L	+S	+L	+S	+L	+S	+L	+T	0S	+L	+T	0S	+L	+T	0S	+L	+T
Acid-fast saprophyte "Day"	+S	+L	+S	+L	+S	+L	+S	+L	+T	0S	+L	+T	0S	+L	+T	0S	+L	+T

* The addition of 1 per cent dextrose promoted growth with fine suspension planting up to concentrations of 10 to 50 units of streptomycin per cubic centimeter.

† S indicates 1 mg. per cubic centimeter fine suspension planting; L indicates planting of divided particles of bacillary mass directly from another culture; 0 means absence of growth; + means growth.

‡ The growth obtained from subcultures grown on 50 units streptomycin per cubic centimeter were transferred to streptomycin-containing mediums, and the direct results from these first transfers are indicated as +T or +T.

§ No. 4038, H 168 and H 37/rv grew less vigorously on this medium than the other strains, although they grew equally well on good nutrient mediums.

11. Corper, H. J., and Vidal, C. B.: The Inhibitory Effect of Normal Blood on the Growth of Tubercle Bacilli at Incubator Temperature, Am. Rev. Tuberc. 33:573-581, 1935.

phyte "Day," which was prepared in a fine suspension containing 1 mg. per cubic centimeter. Growth occurred on all the organs as such—lung, liver, spleen and kidney—and in the saline dilutions, suggesting an absence of demonstrable retarding concentrations of streptomycin in these organs following both intravenous and subcutaneous injection. Chemical assay methods, though tried by us, have proved completely unreliable for determining small amounts of streptomycin in the tissues.

THE EFFECT OF STREPTOMYCIN ON TUBERCULOSIS

Any consideration of the effect exerted by streptomycin on tuberculosis or on the tubercle bacillus in vivo resolves itself into the solution of three phases of the problem: whether streptomycin can kill tubercle bacilli in the host, whether it can completely retard the development of either the tubercle bacilli or the tuberculosis and, if not, whether it can partially retard them. The resolution of tuberculosis within a reasonable time is involved in the foregoing three phases, as is evident from any morphologic study with either dead or avirulent tubercle bacilli, and requires separate consideration.

TABLE 3.—*The Growth of Acid-Fast Bacilli on Tissues and Body Fluids* and the Effect of Streptomycin*

Body Fluid or Tissue	Growth with Given Concentration of Streptomycin†				
	0	1	5	10	100
Citrated plasma					
Full strength	+	+	+	+	0
1:1 (Wong's medium)	+	+	+	+	0
1:10 (Wong's medium)	+	+	+	+	0
Blood sediment (RBC)					
Full strength	0	0	0	0	0
1:1 (Wong's medium)	+	+	+	+	0
1:10 (Wong's medium)	+	+	+	+	0
Lung					
1:1 solution of sodium chloride	+	+	+	0	0
Liver					
1:1 solution of sodium chloride	+	+	0	0	0
Spleen					
1:1 solution of sodium chloride	+	+	0	0	0
Kidney					
1:1 solution of sodium chloride	+	+	+	0	0

* A fine suspension containing 1 mg. per cubic centimeter of a growth of acid-fast saprophyte "Day" as test organism was planted in the various mediums.

† The concentration is given as units per cubic centimeter.

In order to note the action of streptomycin on virulent tubercle bacilli in vivo, animals were infected and treated at various periods for prolonged intervals, after which they were examined for viable tubercle bacilli and tuberculosis. In table 4 the condensed results of extensive studies of the various phases of this problem are presented.

It is noted from the data recorded in table 4 that prolonged streptomycin treatment retarded the tuberculosis but did not prevent death of the guinea pigs from tuberculosis. Positive cultures of virulent tubercle bacilli were obtained from all the important organs, regardless of whether the animal had received as little as 0.1 mg. of bacilli intravenously and had lived under treatment for as long as one hundred and eighty-one days. It was interesting to note also that if treatment was begun only one week after intravenous infection, after which the disease becomes established in the organs, the animal ultimately dies of generalized massive tuberculosis. An interesting feature of this experiment was that some of the guinea pigs taken off treatment after forty days survived almost as long as those treated continuously until death. Without going too far into interpretation, it appears that the streptomycin exerts its initial and potent effect at the time of infection, or coincidentally with it, and that the establishment of immunity is a potent factor in the prevention of spread of the disease and delays death of the animal. This is further emphasized when the animal has been infected subcutaneously and treatment initiated with large doses of streptomycin after tuberculosis has become well established in the organs. In this case the streptomycin proves more toxic to these animals, which is evident from the fact that some of the animals

TABLE 4.—*The Effect of Streptomycin Treatment on Guinea Pigs Infected Intravenously with 1 Mg. of Virulent Human Tubercle Bacilli (No. 4008)*

Interval After Infection When Animal Was Examined	Streptomycin Treatment	Results of Culture of Organs				
		Lung	Liver	Spleen	Kidney	Brain
1 day (animal killed)	Control—no treatment	3*	4	3	4	5
3 weeks (animal died)	Control—no treatment	2	3	3	3	2
27 days (animal died)†	12,000 units daily throughout	2	3	2	2	.
115 days (animal died)	Treatment begun 1 week after infection, 25,000 units daily until death	Massive tuberculous involvement of all important organs				
152 days (animal died)†	12,000 units daily throughout	3	4	3	4	3
181 days (animal killed)†	12,000 units daily throughout	7	4	3	5	..

*The numeral indicates the number of weeks at the end of which positive cultures were obtained on glycerin-egg yolk medium.

Virulence tests of the strain recovered from these animals disclosed no change of virulence beyond that disclosed on the same strain when it was inoculated into these animals. Both in vitro and in vivo resistance tests were performed. The in vivo treatment experiments with streptomycin revealed an increased resistance to the effect of the streptomycin following passage through the streptomycin-treated animals.

Those guinea pigs had been vaccinated with 1 mg. avirulent human tubercle bacilli one month prior to infection and the animal killed at one hundred and eighty-one days was the longest survivor.

succumb acutely with the initiation of treatment. Surviving this, they appear to reveal a retarding effect; but because of the marked variation in the results of infecting groups of such animals subcutaneously, no definite resolution of the disease is demonstrable.

In order to determine the effect of streptomycin on the viability of an avirulent strain of tubercle bacilli,

TABLE 5.—*The Effect of Streptomycin Treatment on the Organic Distribution and the Viability of Avirulent Human Tubercle Bacilli Injected Intravenously*

Interval After Infection When Animal Was Examined*	Streptomycin Treatment	Results of Culture of Organs†					
		Lung	Liver	Spleen	Kidney	Brain	Bone Marrow
1 month	No treatment	3†	3	3	4	0	3
100 days	No treatment	4	4	4	4	0	0
100 days	25,000 units daily throughout	5	4	4	4	5	6

* These animals weighed about 300 Gm. when given 1 mg. of viable avirulent human tubercle bacilli intravenously. They showed no apparent detrimental effect on their growth as compared with normal and streptomycin-treated controls.

† The numeral indicates the number of weeks that elapsed before a positive culture for tubercle bacilli resulted.

which are naturally destroyed in the guinea pig in about one year after the intravenous injection of approximately 1 mg. of a fine suspension of bacilli, young guinea pigs were given intravenous injections of 1 mg.

of an actively growing young culture of avirulent human tubercle bacilli, and some were treated with streptomycin while others were not treated. The organs were cultured, and the results are recorded in table 5.

The findings recorded in table 5 indicate definitely that intensive streptomycin treatment begun at the time of injection of viable avirulent human tubercle bacilli and continued for one hundred days exerts no appreciable effect on the viability of these avirulent tubercle bacilli in the various organs of the guinea pig even though the bacilli are present there in only relatively small numbers and naturally tend to be destroyed in these organs.

AN ATTEMPT TO DETERMINE THE MECHANISM BY WHICH TUBERCULOSIS IS RETARDED AFTER INJECTION OF STREPTOMYCIN

From all that has been determined with regard to the mechanism of the action of streptomycin in tuberculosis, it would appear that the general assumption is that it acts in the human being as it does in the test tube in vitro—as a bacteriostatic agent that retards the development of the tubercle bacilli or of tuberculosis or of both in the body. However, if it acts thus alone, there are in this explanation a number of voids which require further elucidation. It has not been demonstrated authentically that the streptomycin reaches the tubercle bacillus or the tubercle in active concentration or that it actually responds to all the requirements of true chemotherapy, since it should display either cidal action in some concentration or at some interval of time, or at least prove to be completely retardant of bacillary development in vivo under suitable in vivo set tests. Streptomycin does not do this. Even its retardant capacities were incomplete and fluctuated under the conditions of our experiment. It is not too much to expect that a drug which exerts such a profound effect on tuberculosis as is recorded clinically for man from some observations should yield equally clearcut abolition in the laboratory animal, in which the conditions of test can be controlled. At least it is well to determine the limitations of any new therapy. With this in mind, a few variations of tests have been tried in the hope of gaining a better insight into the action of streptomycin and, by comparison, elaborating on its chemotherapeutic action. We have been unable to prevent a lethal outcome of tuberculosis in animals by the use of streptomycin, although we have been able to delay that issue. Likewise, with regard to the tuberculin test, no effect of streptomycin treatment has been noted on the local intracutaneous tuberculin reaction, which indicates the presence of tuberculoallergic hypersensitiveness, either in immune or in nonimmune, infected guinea pigs. Some of the animals were immunized with 1 mg. of avirulent human tubercle bacilli, injected subcutaneously, and some were not, and all were infected with a virulent strain of human tubercle bacilli one to two months later and then treated continuously with 25,000 units of streptomycin subcutaneously daily throughout infection. The tuberculin tests were regularly recorded as showing 2 to 4 plus reactions to specific amounts of pure tuberculin, becoming more accentuated as time of infection and treatment increased.

In view of the known facts regarding streptomycin, its preparation, chemical structure and excretion, as well as its in vitro action as a retardant readily removed from the bacilli, it appeared advisable to study the occurrence of a delayed action in the animal and the possibility of the occurrence of some indirect effect on tuberculosis. Such studies have disclosed that even though streptomycin appears to leave the blood fairly rapidly after injection and cannot be discerned in the organs or in tuberculous tissues, guinea pigs treated for eighty-two to ninety-one days with 25,000 units of streptomycin daily and then infected intravenously with 1 mg. of virulent human tubercle bacilli in fine suspension one day after discontinuance of treatment, when streptomycin is not determinable in the blood, showed an increase of twenty-nine days in average duration of life as compared with the untreated controls, whose average was twenty-two days.

In another set of experiments in which treatment was instituted at the time of intravenous injection of 1 mg. of virulent human tubercle bacilli in fine suspension, a single subcutaneous injection of 25,000 units of streptomycin being given daily, a definite retardation of the tuberculosis occurred, comparable to that obtained by spacing injections so that four to six were made daily, totaling the same number of units. In the light of the data reported concerning excretion it appears that such an effect of a single daily injection of streptomycin could not be attributed entirely to the retardant effect of the drug on the bacilli. If again one is permitted to compare in vitro action, which obviously must be carefully interpreted, it has been found that growth of tubercle bacilli on liquid or good nutrient solid mediums is dependent on the amount of daily incubation at 37 C., so that, compared with controls continuously incubated at 37 C., cultures incubated for two thirds of the day are retarded only slightly, while those incubated only one third of the day, though growing perceptibly as compared with cultures kept continuously at room temperature (25 C.), show a decided retardation of growth as compared with the incubator (37 C.) cultures. According to prevalent observations, streptomycin remains in the blood for from four to twelve hours after a single injection.

Advantage is taken here of some observations made with a synthetic chemical agent of known composition, not an antibiotic. It is obtainable in chemically pure form, and acts as a retardant in vitro but fails completely in vivo in spite of the fact that it has a consistent retardant potency for acid-fast bacilli and tubercle bacilli in liquid nutrient mediums, regardless of composition of the medium, of 0.000,001 per cent for tubercle bacilli, while streptomycin is retardant only to 0.0001 per cent. It also is recoverable from the blood and the urine in amounts active against acid-fast bacilli after injection, but not from tissues except when added in vitro. The complete details concerning this compound will be reported later. When intravenously infected animals are treated intensely every two hours with almost as much of this compound as the daily amount of streptomycin used, one is surprised, considering the greater in vitro potency of this chemical compound as a retardant, to find that it does not retard the tuberculosis in the guinea pigs. On the contrary, not only do the treated animals reveal a generalized disease, surviving only as long as the controls, but the tuberculous spleens present a darker hue and an apparent increase in size over the controls. This is in contrast to the almost normal color of the spleen of the streptomycin-treated animal. To check these observations further, the effect of this compound and that of streptomycin were studied in normal mice and mice given intravenous injections of 5 mg. of heat-killed tubercle

bacilli in fine suspension. The purpose was to study the effect of these drugs on the tubercle or the cellular tissue reaction produced by dead bacilli. At the end of two weeks the animals were examined, with the results recorded in table 6.

It is noted from the findings recorded in table 6 that streptomycin significantly retards the splenomegaly produced by heat-killed tubercle bacilli injected intravenously, in fine suspensions, into mice. The pure chemical substance that is retardant for acid-fast and tubercle bacilli, on the other hand, produces splenomegaly, not only in the normal mouse but also in the animal given dead tubercle bacilli intravenously.

TABLE 6.—*The Effect of Streptomycin Compared with That of a Chemical Retardant on the Splenomegaly Produced in Mice by Dead Tubercle Bacilli*

Type of Animals	Streptomycin Treatment	Splenic Weight *	Chemical Retardant Treatment	Splenic Weight *
Normal control.....	.....	199 mg.	.....	207 mg.
Normal mice treated	20 mg. daily for 2 weeks †	196 mg.	20 mg. daily for 2 weeks	280 mg.
Mice given 5 mg. heat-killed tubercle bacilli intravenously	.....	388 mg.	.....	438 mg.
Mice given 5 mg. heat-killed tubercle bacilli intravenously and then treated	20 mg. daily for 2 weeks †	224 mg.	20 mg. daily for 2 weeks	676 mg.

* The average weight of the spleens is given.
† One and twenty-five hundredths grams of streptomycin equals 1,000,000 units.

SUMMARY AND CONCLUSIONS

In view of the evidence submitted here, streptomycin cannot be considered a cure for tuberculosis in man at present, since it did not destroy virulent human tubercle bacilli, nor did it completely retard their development in vivo.

Streptomycin apparently did not affect the viability of avirulent human tubercle bacilli in vivo.

In our experimental virulent infection, streptomycin did retard tuberculosis but could not prevent a lethal issue of the infection. From evidence available at present, there is no reason to suspect that streptomycin acts differently in man than in animals. None of the animals treated with streptomycin in our tests escaped the lethal issue after the development of virulent infection.

The intimate mechanism by which streptomycin acts in vivo is not fully understood. However, by way of comparison, a pure synthetic chemical substance which acts efficiently in vitro on the growth of tubercle bacilli and acid-fast bacilli and which, after injection in vivo, is demonstrated in the body fluids and the urine in active form was found not to be a retardant of experimental tuberculosis. The difference in action between the two materials in vivo is exemplified by the different splenic tissue reactions noted.

On the basis of evidence presented here and the unstable in vitro retarding unit value of streptomycin in simple mediums for acid-fast and tubercle bacilli, it appears desirable to obtain more controlled evidence before accepting streptomycin as more than incompletely retardant of tuberculosis in man.

The commercial availability of streptomycin should not interfere with additional controlled scientific investigations based on the knowledge gained through the study of this antibiotic.

ABSTRACT OF DISCUSSION

DR. EMIL BOGEN, Los Angeles: Dr. Corper has again reported valuable experiments relating to the bacteriology of tuberculosis and the effect exerted by the tubercle bacillus on experimental animals. Many of the experiments are consistent with those made in our laboratory, which have been reported. In regard to others, we have had marked differences; I must differ particularly in consideration of the clinical interpretation which has been made. Streptomycin is a retardant rather than a bactericidal agent. The tubercle bacillus can be kept from growing, without being actually killed, over a wide range of concentrations of streptomycin. But this retarding action may be of considerable importance in saving lives. We have many guinea pigs surviving after treatment with streptomycin whereas the controls similarly inoculated died many months before. Guinea pigs treated with large doses of streptomycin show minimal lesions; in some cases we have not been able to find any lesions where the controls were riddled with the infection. Similarly, many patients now show complete healing of tuberculous lesions which had previously existed, whereas control patients with similar lesions still show persistence of such lesions. It is important that medicine have more experimental evidence, both in the test tube and in experimental animals, of the extent and the manner of effect of streptomycin and of the other substances which we hope will soon be developed for this purpose. But we must be happy that at last one substance has been found which, not only in the test tube and in experimental animals but also in the clinic, shows the value of experimental research in the chemotherapy of tuberculosis.

DR. H. J. CORPER, Denver: There is no discrepancy between some of these things. We notice drug houses have wisely put out streptomycin as an adjuvant and advise also continuing sanatorium treatment, and I think that is wise in view of what we know.

Clinical Notes, Suggestions and New Instruments

NEOSTIGMINE TOXICITY
Report of Fatality Following Diagnostic Test for Myasthenia Gravis

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Since the introduction of neostigmine as an aid in the diagnosis of myasthenia gravis,[1] it has been widely used for this purpose. Its injection in small doses is generally regarded as a relatively safe procedure. No reports of fatal reactions to its diagnostic use are found in the literature.

REPORT OF A CASE

A white man aged 39 consulted his physician because of generalized weakness for about two months. The history and physical examination were not remarkable except for some ptosis of the eyelids. As a therapeutic test for myasthenia gravis, 1 cc. of a 1:2,000 solution of neostigmine methylsulfate [2] was injected intramuscularly. No changes were noted for the first few minutes after injection. Then a generalized convulsive seizure occurred, five minutes after the administration of the neostigmine.

No fasciculations were noted at this time. Ten minutes after the injection, salivation and respiratory difficulty were noted, and the patient began to show signs of shock. Fifteen minutes after the injection, the pulse rate was found to be only 10 per minute, and the respiration was so depressed that artificial respiration was started. The shocklike state continued. Atropine sulfate, 0.4 mg. (gr. 1/150), and nikethamide were injected twenty-five minutes after the injection of the neostigmine

From the Office of the Chief Medical Examiner, Baltimore, and the Department of Medicine, Johns Hopkins University.

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2. Prepared by Hoffman-LaRoche, Inc

After this, the patient rallied somewhat, the salivation became less pronounced and the respiration and pulse improved. The pulse rate rose from 10 to 20 per minute. The injection of atropine was repeated in twenty minutes, but the patient gradually lapsed deeper into shock. The pulse became slower, the respiration more labored and the salivation and frothing more pronounced. Death occurred fifty minutes after the diagnostic injection of the 0.5 mg. of neostigmine.

At postmortem examination, the face was cyanotic. No other abnormalities were found on external examination. The body cavities were normal. The thymic remnant was somewhat larger than that usually seen. The heart was normal except for mild coronary arteriosclerosis. There was no coronary obstruction at any point, and no valvular or myocardial lesions. The lungs were hyperemic and extremely edematous, with frothy blood-tinged fluid streaming from the cut surfaces of all the lobes of both lungs. The bronchi and trachea were filled with frothy fluid. The spleen, liver and kidneys were decidedly hyperemic. The brain was normal except for considerable vascular engorgement and an increased amount of subarachnoid fluid. No other abnormalities were found. Microscopic examination confirmed the gross findings. In summary, the most striking finding at autopsy was the intense vascular engorgement occurring diffusely throughout the body, resulting in widespread capillary dilatation, edema and hyperemia of all the organs. These changes are of course characteristic of shock from any cause.

The materials used for injection were carefully investigated, to rule out any possibility of error in the strength of the solution or the technic of administration. The solution remaining in the vial used for the injection was assayed, by Mazur and Bodansky's[2] modification of Ammon's [4] method for assaying cholinesterase activity. The cholinesterase activity of this and other ampules from the same lot, tested against normal human plasma and compared with neostigmine samples of known strength, indicated that the solution used was in the proper concentration of 0.5 mg. per cubic centimeter.[5] This established the fact that only 0.5 mg. of neostigmine methylsulfate was actually injected.

COMMENT

In this case, the dramatic course of events following the injection of neostigmine suggests that the death was due to uncontrolled anticholinesterase activity. With the normal cholinesterase activity inhibited by the neostigmine, the action of acetylcholine was unopposed. A fatal vagotonic shock resulted. The microscopic pathologic changes agreed closely with those described by Altschul and Laskin[6] in their animals dying of overdosage of acetylcholine.

This profound physiologic disturbance from such a small amount of neostigmine is difficult to explain. Altschul[7] found a considerable variation in individual susceptibility to this drug in experimental animals. Possibly similar variations in susceptibility exist among the human population. Another factor is the convulsion that ushered in the untoward symptoms in this case. It is possible that the excessive neuromuscular activity occurring in a convulsive seizure produced an overwhelming amount of acetylcholine. Since cholinesterase normally destroys acetylcholine and since the cholinesterase in this case was inhibited by the neostigmine, the body was poorly prepared to cope with any increased production of acetylcholine. The acetylcholine could then accumulate in the body until it reached a concentration sufficient to induce shock. This case has certain similarities to the nearly fatal case described by Goodman and Bruckner,[8] in which muscular exercise apparently increased the acetylcholine concentration to a degree that was dangerous in proportion to the neostigmine-inhibited cholinesterase. The excessive neuromuscular activity of a convulsive seizure would doubtless liberate more acetylcholine than the walking in Goodman and Bruckner's case. The sudden onset of a convulsive seizure in a man previously free of such phenomena is of course unexplained.

Whatever the exact mechanism of the untoward result of administration of neostigmine in this case, the inescapable conclusion is, as Goodman and Gilman[9] pointed out, that the use of neostigmine demands caution and respect.

STREPTOMYCIN AND SULFADIAZINE (COMBINED) IN CHRONIC BRUCELLOSIS

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The following report is made at this time because of the favorable effect of adequate dosage of streptomycin and sulfadiazine given concomitantly to a patient suffering from chronic brucellosis due to Brucella suis infection and because there is little in the current literature on the combined use of streptomycin and sulfadiazine in Brucella infection. Also it seems of value to call attention again to the fact that the hog variety of Brucella (Br. suis) is not confined to the hog-raising regions of the United States.

Sulfadiazine or other sulfonamide compounds have not proved effective in an impressive percentage of cases of chronic brucellosis, although there is much evidence that they may be effective in the acute infection. Even in the acute illness relapse frequently follows discontinuance of the sulfonamide compound.

Streptomycin is not generally accepted as effective against Brucella in vivo, perhaps because of the inconclusive early reports [1] of its failure to bring about definitive results. It is possible that these early reports were based on inadequate dosage or on insufficiently prolonged treatment, or both, as mentioned in the reports themselves. Also it is probable that there is additive effect when streptomycin is administered in conjunction with sulfadiazine, and perhaps with other sulfonamide compounds.

The apparently successful treatment of 2 patients with acute brucellosis by combined use of sulfadiazine and streptomycin was reported by Pulaski and Amspacher.[2] In a later personal communication they [3] reported similar results in 3 of 4 additional cases. The fourth patient recovered but in a manner which suggested spontaneous remission, they thought. Eisele and McCullough [4] reported successful treatment of an acutely ill patient.

In July 1947 the first opportunity was presented to evaluate the method in a chronic Brucella infection.

REPORT OF CASE

A farmer aged 42 years living in southern Maryland complained of fatigue, sweating, epigastric discomfort and severe headache in September 1946. Symptoms had recurred at irregular intervals for several weeks, but headache had been rather constant, coming on at about 9 or 10 a. m. and persisting until about 4 p. m. daily. The temperature ranged from 99 to 100.8 F. Other likely causes for his illness having been excluded, brucellosis was strongly suspected. Blood agglutination reaction with Brucella was positive in a dilution of 1:1,280 on September 28. Other laboratory study was negative or noninformative, as was physical examination.

He was referred by one of us (P. C. J.) to the other (H. J. H.) on October 7 for confirmation of diagnosis and for advice as

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2. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy for Certain Infections of Intestinal Origin, New England J. Med. **237**: 419-428 (Sept. 18) 1947.
3. Pulaski, E. J., and Amspacher, W. H.: Personal communication to the authors, Oct. 8, 1947.
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to treatment. He was a well developed, healthy-looking man and did not appear really ill. In fact, he stated only that he was "a little damp," and mentioned briefly that he had "neuralgic headaches and stomach upsets." It required questioning to bring out that fatigue had been great and that he had had a stiff elbow for a month or two in February, with no swelling, redness or local heat. Also he recalled that he had been stiff all summer after heavy lifting, and that sexual desire had lessened.

He had been born in southern Maryland and had always lived on a farm in that region. There had been practically no illnesses except for "a touch of pneumonia three or four years ago." His cattle had never aborted or been suspected of having Bang's disease. The small herd of 12 or 13 cows had recently showed negative blood agglutination reactions. However, abortion had occurred among his swine; 1 sow had lost two successive litters in March and June, each time about half way through the gestation period. Interestingly the hogs had been in the same pasture with the cows in which no apparent infection developed. Raw milk was used from these cows.

Physical examination on October 7 revealed no significant abnormality. He was 71 inches (180.3 cm.) tall and weighed 181 pounds (82.1 Kg.). The spleen was not palpable. His pulse rate was 88, his temperature 100 F. and his blood pressure 120 systolic and 62 diastolic. Hemoglobin was 90 per cent (14.6 Gm.) (determined by the Dare method); the red blood cell count was 4,350,000, white blood cell count 5,500, with 46 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 51 per cent lymphocytes and 1 per cent basophils. The sedimentation rate was 45 mm. per hour (Westergren method). Microscopic blood agglutination reaction with Br. abortus was complete in 1:40 and 1:80 dilutions (tests in higher dilutions were not carried out by this method). Macroscopic tube agglutination reaction was positive in a 1:640 dilution. Opsonocytophagic reaction showed pronounced phagocytosis in 0 cells, moderate in 0 cells, slight in 17 cells and none in 8 cells, a Foshay numerical index of 17. No cutaneous test had been performed to date, but was then done, 0.1 cc. of "brucellergen" 1:12,000 dilution intradermally in one arm and 0.1 cc. of heat-killed Br. abortus organisms in the other arm. The "brucellergen" reaction was negative at the end of twenty-four and forty-eight hours and subsequently. Reaction to heat-killed Br. abortus organisms was positive.

Blood culture yielded Br. suis. Studies of susceptibility to streptomycin showed that the organism was susceptible to 1 unit of streptomycin; i. e., it was five times as resistant as standard.

Intramuscular administration of Br. abortus vaccine in any dilution necessary to avoid more than slight local, focal or systemic reaction was advised as a preliminary method of treatment, with the reservation that failure of complete recovery might occur. In that event it was suggested that streptomycin and sulfadiazine should then be administered, simultaneously, in adequate dosage and over a period of about twenty-one days. Vaccine was administered in a dilution of 1:100, intramuscularly, beginning with 0.1 cc. on October 22 and ending on November 8. Increments used were 0.1 to 0.4 cc., at intervals of three to six days, instead of the usual smaller increments and intervals of four to seven days. There were no apparent reactions to the five doses of vaccine given except for slight additonal elevation of temperature following the first two doses and lowering of fever curve following each of the latter three doses. After this regimen the patient resumed his farm work, improved but not fully recovered, still with a temperature ranging from 99.8 to 100.8 F. each afternoon. On one occasion in November the spleen was felt.

In July 1947, about one year after the onset of symptoms referable to brucellosis, because of continued low grade fever, fatigue and muscle and articular pains, the original plan for use of streptomycin parenterally and sulfadiazine orally was put into effect. Treatment was begun with 4 Gm. of streptomycin and 6 Gm. of sulfadiazine daily. After five days of this dosage of streptomycin it was reduced to 2 Gm. daily for three days and then to 1 Gm. daily for the remainder of the period of nineteen days. A total of 44 Gm. of streptomycin was used. The dosage of sulfadiazine was sufficient to keep the blood level between 5.9 and 6.3 mg. The amount of streptomycin used was less than planned because of the improvement which was evident at the end of forty-eight hours, at which time the patient was entirely free of fever and all symptoms.

There were no noticeable toxic effects from this dosage of streptomycin. It had been planned to discontinue its use at once if symptoms referable to involvement of the eighth nerve became evident.

The patient has remained afebrile and symptomless for four months, except for an unrelated sinus infection in November 1947. Blood culture for Brucella was negative at that time.

SUMMARY

So far as is known, this is the first reported case of chronic brucellosis successfully treated with streptomycin and sulfadiazine, concomitantly. The following points have been brought out: A man aged 42 years suffering from chronic brucellosis due to Br. suis showed few physical changes. There was low grade fever, slight leukopenia with relative lymphocytosis, blood agglutination reaction with Brucella in high titer, slight phagocytic activity of the white cells, positive intradermal reaction to Br. abortus killed organisms but negative intradermal reaction to "brucellergen," and positive blood culture. The increased erythrocyte sedimentation rate was of interest because it is not usual in uncomplicated Brucella infections. Also unusual was the moderate degree of intradermal reaction to killed Br. abortus organisms in a farmer whose exposure presumably had been by direct contact with infected animals. Particularly significant but not uncommon was the lack of cutaneous sensitivity to "brucellergen" but characteristic reaction to a more sensitive antigen, heat-killed Br. abortus organisms. Also of interest was the fact that the organism recovered was of the hog variety although originating in the Eastern United States.

The phagocytic reaction in this patient would be classified as "negative" by those who believe that phagocytic indexes as high as 30 may occur in blood of "normal" persons, although in fact low degrees of phagocytic activity against Brucella are a common finding regardless of the severity of infection. Had "brucellergen" been the only skin-testing antigen used, as is often the case, a negative reaction would have resulted. Had specific agglutinins not been present in high titer, the diagnosis then would have rested on blood culture alone—a procedure for which few laboratories have proper facilities or trained personnel. In this chronic illness there was the unusual good fortune to have adequate diagnostic data.

Whereas relapse still may occur, the complete freedom from any evidence of Brucella infection for a period of four months after specific treatment, following one year of chronic illness, seems sufficiently significant to justify further attempts at evaluation of this combined form of chemotherapy in acute or chronic brucellosis. Prolonged dosage of both drugs seems indicated, with sufficiently high initial dose to avoid the likelihood of resistance to streptomycin. Due regard to possible toxic effects obviously is necessary.

Painless Coronary Infarction.—Clinical statistics are presented which indicate that all suitable cases of angina pectoris can be relieved of their crushing precordial and arm pain by properly executed neurosurgical procedures. These patients do not lose the danger signal which warns against over-exertion, but it is no longer agonizing pain. In skilled hands surgical intervention is no more dangerous than any of the other common major operations in this age group. Once relieved of their pain, these patients are able to live happier and more active lives, free from fear of ever-recurring attacks and less conscious of impending death. They are no longer threatened with addiction to morphine, lack of sleep, and worry, which so often are factors accelerating termination of life by coronary occlusion. If fatal coronary infarction takes place, it is usually painless.—White, James C., and Bland, Edward F.: *Medicine*, February 1948.

Council on Pharmacy and Chemistry

The Council has authorized publication of the following statement.

AUSTIN SMITH, M.D., *Secretary.*

Report to the Council on Pharmacy and Chemistry by the Committee on Drug Addiction and Narcotics of the National Research Council, prepared for the committee by Dr. Nathan B. Eddy, Secretary.

METOPON HYDROCHLORIDE

(Methyldihydromorphinone Hydrochloride)

Metopon (or methyldihydromorphinone) represents a new type of nuclear substitution in the morphine series for which the method of preparation was discovered by Small in 1936. The essential difference in metopon is the presence of a methyl group attached to the hydroaromatic ring of morphine. It also differs from morphine by the presence of a ketone in place of the alcoholic hydroxyl and by removal of one double bond by hydrogenation. Pharmacologic examination and clinical trial demonstrated that these chemical changes effected quantitative dissociation of components of the morphine picture - increase in analgesic action, decrease in euphoric, sedative, emetic and intestinal effects. Tolerance to and dependence on metopon developed more slowly and tolerance disappeared more rapidly than with morphine. Substituted for morphine in cases of addiction, it did not fully satisfy the craving or completely suppress abstinence phenomena. The minimal analgesic dose, the incidence of adequate relief and of side actions, and the duration of action were the same for oral and hypodermic doses administered for the relief of clinical pain.

Fig. 1.—Structural formulas of metopon (methyldihydromorphinone) on the left and morphine on the right.

In review of the evidence on metopon in 1946 the Drug Addiction Committee of the National Research Council judged that in comparison with morphine the differences already outlined were clearly demonstrated. The Committee believed that these differences indicated the possibility of advantageous employment of the drug by the oral route for the control of chronic pain such as that in cancer. To test this possibility they recommended limited commercial production and distribution of metopon under a plan of supervision which would channel the drug to cancer patients only and which would seek to gather reports on its effectiveness for such cases in general practice. The plan of supervision has been published,* and this report reviews the first six months of its operation from May 15 to Nov. 15, 1947.

Figure 2 presents a graph of the amount of metopon distributed on original orders and reorders. Two thousand, eight hundred and twenty-nine physicians have ordered the drug for 4,288 patients. As of November 15, 20 per cent of all physicians who had ordered metopon had reordered and 33 per cent of these had reordered more than once. Both these figures are lower than the true extent to which physicians are reordering, since the figure for physicians ordering initially is also compiled to November 15 and obviously some proportion on that date had not yet received the drug and a larger number had used it too short a time to reorder. One hundred and six reorders were received in the three week period November 15 to December 5; fifty-five were from physicians reordering for the first time. In other words, as of December 5, 21.8 per cent of the physicians who had ordered metopon by November 15 had reordered at least once, which certainly represents only a partial correction for the time factor. Another estimate of the continuing use of the drug is derived from physicians' reports. Three hundred and forty, or 12 per cent, of physicians have reported on or signified their intent to use metopon for 461 additional patients, approximately 11 per cent of the number for whom the drug was ordered originally.

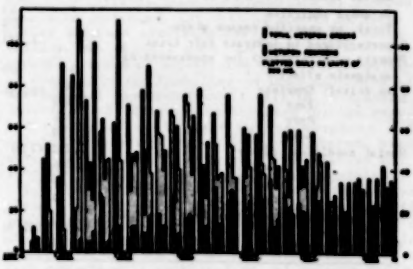


Fig. 2.—Amount of metopon distributed on orders and reorders.

Only eighteen orders for metopon have been rejected because the case for which it was intended was not one of cancer, cancer being interpreted in a broad sense to include all types of malignant tumor. A few physicians have asked or have tried to use the drug on other patients in addition to 1 or more patients with cancer, but to the best of our knowledge the drug has been sought for only 43 noncancerous patients, only 1 per cent of the total. Only ten other original orders have been rejected either because a satisfactory statement in regard to the diagnosis or the attending physician has not been supplied or because the narcotic order has been improperly executed. In each instance an effort was made to get the information or to have the error corrected before the order was rejected.

One of the requirements of the Committee's program of supervision is that a reorder shall be filled only after the physician has reported on the use of metopon. One hundred and one physicians have overlooked this requirement, but most have responded promptly when reminded of it. Only eleven reorders have been rejected because we were unable to get a report. Some reorders are received with which the physician states that he intends the drug for a new patient. Such reorders are approved whether or not the physician has reported, though he is asked again under these circumstances for a report on each case and usually responds promptly.

Practically all the cancer patients for whom metopon has been sought were in the terminal stage of recurrence and/or metastasis. Two hundred and twenty-seven, or 5 per cent, are known to have died before the drug could be received. Physicians have reported nonuse of the drug after ordering in 131 other cases, principally because other medical care was obtained, the patient moved from the locality or there was a recession in the pain of the disease. Correcting the total number for deaths, nonuse and noncancerous cases, metopon is presumed to have been used for 3,887 patients. This figure is undoubtedly too high, because deaths and nonuse certainly were not reported completely. Physicians have reported on the use of the drug in 1,841 cases. Some effort is required to attain this response, since four hundred and twenty-six reminder letters have been written and several hundred more are being written now. Reports from two hundred and ninety

*J.A.M.A. 134:291-292, 1947; J. Am. Pharm. A. (Pract. Pharm. Ed.) 8:430-433, 1947. Also in most of the state medical association journals, June to October, 1947.

physicians have been received through these reminders. Tables 1 and 2 present a general summary of all reports.

Table 1.—*General Summary of Reports on the Use of Metopon**

Reasons given for trial of metopon:		
For better pain relief		946
To avoid hypodermic administration		389
Nausea and/or vomiting with morphine or other narcotic		277
Mental dulness with morphine or other narcotic		87
To avoid addiction		63
Trial, no specific reason given		274
Reports judged to indicate fair trial		1,341
Reports unsatisfactory for assessment of analgesic effect		500
Pain relief: Complete	477	(80 %)
Fair	598	
Poor	187	
None	79	
Mental condition: Clear	1,142	(75%)
Dull	286	
"Dopey"	75	
Confused	29	
Sleep promoted or permitted by relief of pain	645	(27 %)
Sleep not promoted	1,192	

*In each table figures represent cases in which the item is reported. Totals for pain relief, mental condition and sleep are uneven because of inadequacy of data on some reports.

Among the reasons given for trial of metopon, "for better pain relief" usually means that tolerance to other narcotics has already developed, since it is always specifically stated for these cases that previous medication was inadequate. Also other narcotics (morphine, codeine, dihydromorphinine, "pantopon" the total alkaloids of opium as soluble hydrochlorides or meperidine, in various sequences or combinations, frequently all of them) have been administered for six months or more in 39 per cent and for two months or more in 72 per cent of all cases for which information on this point is available. There was no narcotic medication prior to metopon in only 74 cases.

Table 2.—*Side Reactions with Metopon*

None	1,592	Disturbing dreams	6
Nausea	87	Itching	4
Restlessness	23	Anorexia	3
Headache	14	Urticaria	2
Perspiration	12	Tinnitus	2
Dryness or burning in throat and stomach	10	Allergic reaction	1
		Edema of face	1
Dizziness	9	Palpitation	1
Euphoria	7	Hiccup	1
Burning of skin and/or hot flushes	6	Difficulty in urination	1
Nausea, previously reported (277), persisting after metopon			27
Signs of physical and psychic dependence for which metopon was discontinued after brief trial			104
Signs of physical dependence disappearing under continued administration of metopon			45

With respect to other reasons for trial of metopon, the figure for "nausea and or vomiting with morphine or other narcotic" is surely too low. Unfortunately, a specific query on this point was not on the protocol sent to physicians to report results. Also there are included under "trial, no specific reason given" all cases in which it is said that the patients were intolerant to morphine or that they wished to avoid side effects, but for whom emetic action is not directly stated.

In table 1 efforts are shown without regard to the dose employed. All reports which show dose and effect, are included in the tally unless attending conditions are described which obviously vitiate the result. These include attempted administration to patients close to death, attempted administration where nothing given by mouth was being retained and cases in which one or at most only a few doses of metopon were given because of the patient's demand for return to hypodermic medication with or without the appearance of signs of physical dependence, the physician admitting that addiction to morphine or other narcotic was the reason for failure. There were 104 cases in which administration of metopon was shortly discontinued because of its failure to satisfy an existing addiction and its inability to prevent the occurrence of abstinence phenomena. Pain relief was admitted to be fair or better in only 25 per cent of this group. On the other hand, 45 cases have been reported in which in spite of the appearance of abstinence phenomena administration of metopon was continued. The withdrawal signs disappeared gradually, and the net result was excellent. It is probable that some of the symptoms listed in table 2 as side reactions were in fact abstinence phenomena. This is especially probable for the symptom of nausea, which frequently did not appear until after several doses of metopon had been given or at about the time after the last dose of the previous narcotic at which one would expect to see the first signs of withdrawal. It is noteworthy that nausea after metopon therapy was reported in only 27 of the 277 patients known to have been nauseated by previous medicaments.

Restlessness as a side effect has been reported in 23 instances. This is in addition to the group previously mentioned in which mental agitation and anxiety as signs of psychic dependence caused the physician to discontinue administration of metopon. Euphoria was noted only in 7 instances. In 73 per cent of the cases metopon was said not to promote sleep. Even when the report indicates that sleep followed its administration, the note is often added that this is probably only secondary to the relief of pain. The retention of mental clarity, the absence of euphoria and general sedation were sometimes considered disadvantageous. Twelve times, although in most instances pain relief was adequate, metopon was discontinued because of lack of sedative effects. Sometimes the physician found it desirable to give a barbiturate or a small dose of another narcotic at bedtime.

The recommended starting dose of metopon for oral administration is not less than 6 mg. This has been clearly stated in all literature on the use of the drug under this program. Cross tolerance among the opiates has also been referred to, and the possibility of cross tolerance to metopon after prolonged administration of morphine and related substances. Such cross tolerance would be expected to require upward adjustment of dosage. Therefore, to facilitate close adjustment of dose to need under varying circumstances the dosage form originally adopted is a capsule containing 3 mg. of metopon hydrochloride and the dose is "two or three capsules to be repeated only on recurrence of pain." It is surprising that physicians have commonly disregarded all dosage recommendations, directing that the capsules be taken singly at least initially. In 28 per cent of all trials the amount of drug per dose has not been increased beyond 3 mg. In 45 per cent of trials administration has started at or has shortly been increased

to 6 mg. In 25 per cent of trials the dose has been increased to 9 mg., but in only 2 per cent has it been increased beyond that level.

Reference has already been made to the extent of narcotic administration prior to trial of metopon. This breaks down readily into three categories: (1) no previous narcotic, 74 cases; (2) narcotic administration for six weeks or less, a period in which relatively little tolerance and dependence will have developed as a rule, 339 cases, and (3) narcotic administration for two months or more, when some tolerance and dependence will almost certainly have developed, 1,200 cases.

Table 3.—*Influence of Previous Narcotic Administration on the Result Obtained with Metopon, 6 Mg. per Dose*

	No Previous Narcotic	Narcotic Administration 6 Wk. or Less	Narcotic Administration 2 Mo. or More
Number of cases	35	152	492
Pain relief:			
Complete	19(54%)	69 (45%)	135 (27%)
Fair	13(37%)	37 (24%)	199 (40%)
Poor	1	30	105
None	2	16	53
Incidence of nausea	0	5 (1:30)	20 (1:24.5)

Using only the results of 6 mg. doses of metopon, table 3 summarizes the influence of the previous medication. Quite definitely the incidence of adequate relief, fair or better, and particularly of complete relief is less the more previous narcotic medication the patient had received. It should be pointed out, however, that there is probably a relation between the duration and severity of the disease, at least the severity of pain as a symptom of the disease, and the extent of previous medication, so that cross tolerance may not entirely account for the difference shown.

The incidence of nausea as a possible side effect increases from none (where there had been no narcotic given prior to metopon) to about once in twenty-four times where there had been the greatest amount of previous medication. This supports the suggestion already made that some of the symptoms listed as side effects were really withdrawal symptoms. It is also possible in line with the statement of the previous paragraph that at least part of the nausea was incidental, related to the advanced stage of the disease and widespread metastases, and not associated with the medicament.

Two hundred and fifty-eight physicians have reported more than once on the effect of metopon in the same patient. In 164 cases the effect was the same at intervals of one to twenty weeks without change in dose; in 24 cases the effect was reported as increased in the second report, and in 70 cases it was diminished. In other words, there is no evidence of tolerance to metopon in 127, or 50 per cent, of cases in which administration is known to have continued for at least four weeks and none in 37, or 14 per cent, of cases of continued administration for eight weeks or more.

In some reports duration of effect is specifically stated as five to ten hours. In many more it is indicated only indirectly by the statement that only two or three doses per day were taken. In a few instances the effect has been reported as brief, one hour or less. In another small group the patients have complained of slowness of onset of pain relief.

In conclusion, this six months of experience with metopon in general practice has confirmed the earlier results of controlled clinical trials. It is an adequate analgesic for severe chronic pain when administered orally, and such administration is attended by a high degree of mental clarity and few side reactions. The satisfactoriness of its use is improved if its administration is begun as soon as the need for a potent analgesic arises, before the administration of morphine and other related substances has led to diminished effectiveness through the development of tolerance. The committee believes that the production of metopon should be continued, but that it should be recommended and made available only for oral administration for chronic pain. On May 15, 1948 the present program of supervision of the distribution of metopon by the Committee on Drug Addiction of the National Research Council will be terminated. Thereafter the drug may be obtained through regular channels in the same way as morphine and related substances. It must be remembered, however, that metopon is a morphine derivative and, like the latter, subject to narcotic regulations.

The drug will continue to be available only in capsule form for oral administration. Since it is important to hold narcotic administration to a minimum, to facilitate this and to permit adjustment of dose to the need of a particular case each capsule will contain 3 mg. of metopon hydrochloride. The minimal effective analgesic dose in nontolerant persons is 6 mg. Therefore, the dose is two capsules for persons who have not taken morphine and related substances previously, and it may be three or more capsules for persons already tolerant to morphine and the like. Institution of treatment with metopon hydrochloride in the latter group should be accompanied by rapid reduction rather than abrupt discontinuance of the previous medication.

The Committee on Drug Addiction and Narcotics of the National Research Council through its secretary (Nathan B. Eddy, National Institute of Health, Bethesda 14, Md.) will be glad to continue its correspondence with physicians in regard to their experience with metopon hydrochloride and to advise them on the use of the drug.

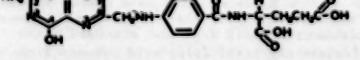
NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

FOLIC ACID.--Pteroylglutamic acid.--N 4 (2-amino-4-hydroxy-6-pteridyl)-methyl -amino - benzoyl glutamic acid.--$C_{19}H_{19}O_6N_7$.--M.W. 441.4.

The structural formula of folic acid may be represented as follows:



Actions and Uses.--(See New and Nonofficial Remedies 1947, p 517).

Dosage.--(See New and Nonofficial Remedies 1947, p 517).

Tests and Standards

Folic acid occurs as a yellowish-orange crystalline powder.

It is insoluble in ethanol, benzene, chloroform, ether and water, although very slightly soluble in hot water.

Dissolve about 5 mg. of folic acid in 5 cc. of glacial acetic acid. Add 1 cc. of 30 per cent hydrogen peroxide and allow to stand for 4 hours: the solution is completely decolorized.

Dry about 0.1 Gm. of folic acid, accurately weighed, in vacuum over phosphorus pentoxide at room temperature in the dark for 120 hours: the loss in weight does not exceed 10 per cent.

Char over a low flame 0.2 Gm. of folic acid, accurately weighed. Cool, then moisten the charred material with 1 cc. sulfuric acid. Cautiously ignite until ashing is complete: the residue does not exceed 0.5 per cent on the anhydrous basis.

Treat the residue from the sulfated ash with 2-3 drops of hydrochloric acid and evaporate to dryness on the steam bath. Add 10 cc. of 2 per cent hydrochloric acid and heat for 5 minutes on the steam bath. Filter through paper into a Nessler tube. Repeat the acid treatment of the residue with 10 cc. more of 2 per cent hydrochloric acid. Dilute to 25 cc., and add 10 cc. of hydrogen sulfide T.S. Allow to stand in the dark for 10 minutes: no more turbidity develops than corresponds to 50 parts per million of lead (U.S.P. XIII).

Place about 100 mg. of para-aminobenzoic acid, accurately weighed, in a 100 cc. volumetric flask, add 50 per cent ethanol to dissolve the solid, and dilute to the mark with 50 per cent ethanol. Transfer 1 cc. of the p-aminobenzoic acid solution to a 250 cc. volumetric flask, add 200 cc. of water, 25 cc. of 5 N hydrochloric acid, 2.5 cc. of a 0.5 per cent gelatin solution (0.5 Gm. gelatin and 0.1 Gm. benzoic acid in 100 cc. water), and finally dilute to the mark with water. Prepare a standard curve, using sufficient solution to give a range of final concentrations of 4 to 20 micrograms, developing the color as described for folic acid as follows:

Weigh, accurately, about 0.1 Gm. of folic acid and transfer to a 100 cc. volumetric flask. Dissolve the folic acid and dilute to the mark with 0.1 N sodium hydroxide. Transfer 1 cc. of the solution to a 100 cc. volumetric flask and add 80 cc. of water, 10 cc. of 5 N hydrochloric acid, 1 cc. of 0.5 per cent gelatin solution, and water to the mark. Withdraw 2 cc. of the mixed solution before reduction and determine the free amine as directed for p-aminobenzoic acid. Transfer the rest of the solution to a 250 cc. Erlenmeyer flask and add 0.5 Gm. of zinc dust. Allow the mixture to stand 10 minutes with intermittent shaking. Filter to free the reduced solution from zinc dust. Pipette 2 cc. of the reduced solution to a 10 cc. volumetric flask. Dilute to 6.6 cc. with water, add 0.4 cc. of 5 N hydrochloric acid and 1 cc. of 0.1 per cent sodium nitrite solution. Mix and let stand 3 minutes and add 1 cc. of 0.5 per cent ammonium sulfamate solution. Mix and let stand 2 minutes, add 1 cc. of a 0.1 per cent N-(1-naphthyl)-ethylenediamine dihydrochloride solution. Mix and allow to stand 5 minutes. Read the light absorption of the solution with a spectrophotometer at 5500 Å, using water as a blank. Determine the concentration of the solution in terms of p-aminobenzoic acid from the standard curve.

Calculate the total folic acid present from the following equation:

$$\text{micrograms as p-aminobenzoic acid} - \text{micrograms free amine} \times \frac{441.4}{137.06} = \text{folic acid found}$$

The folic acid content is not less than 90 per cent on the anhydrous basis.

Folic Acid Tablets

Weigh, accurately, 25 tablets of folic acid. Grind to a fine powder in a mortar and then weigh out an amount equivalent to 100 mg. of folic acid. Transfer the weighed portion to a 100 cc. volumetric flask and dilute to 100 cc. with 0.1 N sodium hydroxide. Centrifuge and transfer 1 cc. to a 100 cc. volumetric flask, and continue the assay for folic acid as described in the preceding paragraphs, beginning with the sentence " Transfer 1 cc. of the solution to a 100 cc. volumetric flask . . .". The folic acid content of the tablets is not less than 90 nor more than 115 per cent.

AMERICAN PHARMACEUTICAL CO., INC., NEW YORK

Tablets Folic Acid: 5 mg.

KREMERS-URBAN CO., MILWAUKEE

Tablets Folic Acid: 5 mg.

LEDERLE LABORATORIES DIVISION, PEARL RIVER, N. Y.

Elixir Folvite: 5 mg. per 4 cc., 125 cc. bottles.

Solution Sodium Folvite: 15 mg. per cc. ampuls.

Tablets Folvite: 5 mg.

U. S. patent pending. Trademark Registered

R. J. STRASENBURGH CO., ROCHESTER, N. Y.

Tablets Folic Acid: 5 mg.

2,3-DIMERCAPTOPROPANOL IN OIL.—BAL in Oil-H. W. & D.—A solution of 2,3-dimercaptopropanol 10 per cent in peanut oil, containing benzyl benzoate 20 per cent.—$C_3H_8OS_2$—M. W. 124.21

Actions and Uses.—2,3-Dimercaptopropanol in oil is indicated in the treatment of arsenic, gold and mercury poisoning.

2,3-Dimercaptopropanol is particularly useful in the treatment of hemorrhagic encephalitis due to massive arsenotherapy, arsenical or gold dermatitis and possibly postarsenical jaundice but not homologous serum jaundice following parenteral therapy. It is useful as an adjunct in the treatment of agranulocytosis due to arsenic, but other measures, principally massive doses of penicillin, must also be employed.

While 2,3-Dimercaptopropanol in oil is indicated in the treatment of mercury poisoning, it must be remembered that mercury causes rapid and extensive tissue damage, particularly to the kidneys, which cannot be corrected by the administration of this drug. The use of 2,3-Dimercaptopropanol in oil in the treatment of mercury poisoning is still in the experimental stage, and definite recommendations cannot be made.

The toxicity of the drug appears to be less in patients suffering from arsenic, gold or mercury poisoning, but doses of 300 mg. per kilogram of body weight may produce nausea, vomiting and headache; a burning sensation of the lips, mouth, throat and eyes; generalized muscular aches with burning and tingling of the extremities, and a sense of constriction in the chest. The symptoms usually subside in thirty to ninety minutes.

Dosage.—In the treatment of arsenic or gold poisoning, 3 mg. per kilogram of 2,3-Dimercaptopropanol (as a 10 per cent solution in oil) should be administered by intramuscular injection as follows: every four hours for the first two days; four injections on the third day, and injections twice daily thereafter for ten days or until complete recovery. In milder cases the dose may be reduced to 2.5 mg. per kilogram.

HYNSON, WESTCOTT & DUNNING, INC., BALTIMORE

Solution Bal in Oil: 4½ cc. ampuls. 2,3-Dimercaptopropanol 10 per cent and benzyl benzoate 20 per cent in peanut oil.

Council on Physical Medicine

ABSTRACT OF MINUTES OF MEETING OF THE COUNCIL ON PHYSICAL MEDICINE

Dec. 12 and 13, 1947

The Council on Physical Medicine held its regular annual meeting on Dec. 12 and 13, 1947. Those present were Drs. Morris A. Bowie, Anthony C. Cipollaro, W. W. Coblentz, John S. Coulter, W. E. Garrey, W. E. Grove, Frank H. Krusen, Frank H. Ober, George Morris Piersol and Derrick Vail. Dr. John S. Coulter was reappointed chairman and Dr. Frank H. Krusen, vice chairman. Dr. Krusen was acting chairman.

Dr. George M. Piersol presented a report from the Consultants on Clinical Thermometry. Two articles are being written on the subject. He stated that the commonly accepted idea about normal clinical temperatures is far from accurate and a report will be available in due time.

The subject of ion transfer employed therapeutically was discussed. The critical evidence is limited, and in the opinion of the Council the problem should be studied further.

With regard to muscle stimulation, the Council believes that there is no necessity for a multiplicity of current combinations in an apparatus, since there is no critical evidence to justify their use.

The Official Rules of the Council on Physical Medicine were discussed and brought up to date. Several minor changes were made in the body of the booklet. Rule 9, "Policies of Firms Detrimental to Rational Therapeutics," was revoked.

The question whether hearing aid manufacturers be allowed to state that a hearing aid is accepted if it meets the requirements (that is, before it is formally accepted) was discussed. It was decided that all manufacturers should adhere to the rules and that no exceptions should be made.

The articles on atomic energy which were assigned to subcommittees of the Consultants on the Medical Aspects of Atomic Energy and Roentgen Rays and Radium have not been received. Dr. Edward Bortz, President of the American Medical Association, in a letter commended the Council on Physical Medicine for its work on atomic energy. He emphasized the importance of informing the members of the medical profession concerning the clinical value of radioactive isotopes and urged a more aggressive educational program. The revision of the glossary of terms used in atomic energy is proceeding.

The Council expressed its willingness to cooperate with the Council on Medical Education and Hospitals in the evaluation of schools for physical therapists and occupational therapists.

The Secretary was instructed to approach the Consultants on Education of the Council in order to formulate recommendations with regard to minimal suggested science requirements for admission to courses in physical therapy. These recommendations will then be presented to the Council on Medical Education and Hospitals.

The Council members voted that the Council on Scientific Assembly consider establishing a permanent Section on Physical Medicine beginning with the association meeting in 1949.

Due to the fact that the Committee on American Health Resorts was disbanded by the Board of trustees, the Council voted to appoint a group of Consultants on American Health Resorts.

The Council reaffirmed its ruling in regard to germicidal lamps as recorded in "Acceptance of Ultraviolet Lamps for Disinfecting Purposes."

In discussing the subject of ultraviolet radiation and cancer, it was revealed that the following two factors are responsible for cancer of the skin: (1) the quality of the radiation 2,900 to 3,200 angstrom units and (2) the quantity of the irradiation.

The use of radium in treating deafness was discussed at length. It was concluded that until definite evidence is adduced that the treatment is dangerous, advertising of such treatment may be continued in the publications of the American Medical Association.

Dr. Henry Schwerma presented a report on the research in artificial respiration which has been supported by a grant from the Board of Trustees.

The work of the Consultants on Contraceptive Devices, Audiometers and Hearing Aids, Electrocardiographs, Electroencephalographs and Respirators was reviewed.

The resignation of Dr. Grove as chairman of the Consultants on Audiometers and Hearing Aids because he is now a member of the Council was accepted with regret. Dr. Hallowell Davis was appointed to fill the vacancy.

The Council voted to disband the group of Consultants on Ophthalmic Devices because the same members serve as the Committee on Optics and Visual Physiology, and it is too large and busy to consider problems coming before the Council. A new group will be appointed.

Dr. Paul Klopsteg reported on the activities of the Consultants on Artificial Limbs. It was the general consensus that the present group is too large to work efficiently, and it was decided to appoint a new group of Consultants on Artificial Limbs. The revision of the Handbook on Amputations is to be postponed until the large book being prepared by the Committee on Artificial Limbs of the National Research Council has been published. Dr. Klopsteg was appointed to prepare an article on the subject of artificial limbs for the general medical profession. Drs. Ober and Dickson were appointed to serve on a committee to study ways and means to improve the training of those who fit artificial limbs.

The Council voted to revise the Handbook of Physical Medicine.

AN APPRECIATION

The Council on Physical Medicine desires to take this opportunity to express its gratitude and appreciation for the services of the following consultants, whose assistance in carrying out the work of the Council has been given so freely during the past year (1947): Drs. Charles Bahn, Alvan L. Barach, A. R. Barnes, Edward Bigg, Raymond Carhart, Milton B. Cohen, Earl Elkins, Alan Feinberg, Clarence J. Gamble, K. G. Hansson, L. G. Hardy, E. D. Hauser, J. S. Hibbin, A. Hollaender, M. Joannides, H. W. Kendell, Margaret Kunde, V. Lespinasse, Alfred Lewy, G. Martin, A. Olsen, Stafford L. Osborne, Howard F. Polley, Mr. Luther Ramer, Drs. Scott N. Reger, Henry Schwerma, Daniel Snydacker and G. De Takats, Miss Eva Thompson, Drs. Khalil G. Wakim, Ralph Waters, Harold Westlake, Paul H. Wosika, Jessie Wright and C. R. Zeiss.

Artificial Limbs.--Drs. Henry H. Kessler, Paul Klopsteg, Harry E. Mock, S. Perry Rogers, Paul B. Steele and Philip Wilson; Messrs. McCarthy Hanger Sr., W. E. Isle, J. B. Korrady, Joseph A. Spievak and David E. Stolpe.

Medical Aspects of Atomic Energy.--Drs. Kenneth S. Cole, L. F. Curtiss, Hymer L. Friedell, Shields Warren and Stafford L. Warren.

Audiometers and Hearing Aids.--Drs. Gordon Berry, Hallowell Davis, Kenneth M. Day, E. P. Fowler, Isaac H. Jones, Dean Lierle, Moses Lurie, Douglas Macfarlan, C. Stewart Nash and Paul E. Sabine.

Clinical Thermometry.--Miss Johanna Busse, Drs. George Crile Jr., Eugene DuBois, Steven M. Horvath, John Talbot and George Thorn.

Contraceptive Devices.--Drs. William W. Greulich, Joseph Hughes and Andrew C. Ivy, Professor Walter J. Meek, Mr. R. R. Olin and Dr. Ephraim Shorr.

Education.--Drs. Frances Baker, Robert I. Bennett, Benjamin Boynton, Earl C. Elkins, F. H. Ewerhardt, Richard Kovacs, Fred B. Moor, W. H. Northway, William Schmidt, Walter M. Solomon, Arthur L. Watkins, George D. Wilson and Walter J. Zeiter.

Electrocardiographs.--Drs. A. R. Barnes, George Fahr, Harold E. B. Pardee, William D. Stroud, Carl J. Wiggers and Frank N. Wilson.

Electroencephalographs.--Drs. Percival Bailey, Edward J. Baldes, Stanley Cobb, Hallowell Davis and Frederic A. Gibbs.

Occupational Therapy.--Drs. Raymond B. Allen, Robert W. Johnson Jr., Winfred Overholser, Howard A. Rusk and William D. Stroud.

Ophthalmic Devices.--Drs. Thomas D. Allen, S. Judd Beach, Conrad Berens, Frederick C. Cordes, Alfred Cowan, Walter B. Lancaster, William H. Luedde, Lawrence T. Post, Avery D. Prangen and Kenneth C. Swan.

Respirators.--Drs. Edward L. Compere, Charles F. McKhann and James L. Wilson.

Roentgen Rays and Radium.--Drs. William E. Chamberlain, Arthur C. Christie, Edwin C. Ernst, Giocchino Failla, Fred M. Hodges, Robert R. Newell, Eugene P. Pendergrass, Ursus V. Portmann, Lauriston S. Taylor and J. L. Weatherwax.

The Council on Physical Medicine has authorized publication of the following reports. HOWARD A. CARTER, *Secretary.*

INTERMITTENT POSITIVE PRESSURE BREATHING

A MEANS OF ADMINISTERING ARTIFICIAL RESPIRATION IN MAN

H. L. MOTLEY, M.D.
A. COURNAND, M.D.
L. WERKO, M.D.
D. T. DRESDALE, M.D.
A. HIMMELSTEIN, M.D.
and
D. W. RICHARDS JR., M.D.
New York

Intermittent positive pressure breathing, produced by artificial means, is brought about by actively raising the pressure in the lungs during inspiration, the expiratory phase being either passive or mediated through an active mechanism creating negative pressure in the lungs (table 1). Effective ventilation may thus be maintained in apneic subjects, and at the same time the Hering-Breuer reflex is stimulated by distention of pulmonary alveoli. According to Drinker,[1] this is the best line of attack for the promptest possible restoration of normal respiratory movements. Intermittent positive pressure breathing may be given by mouth to mouth insufflation, a simple effective method seldom used. A more commonly employed method consists in applying intermittent positive pressure through an anesthesia breathing bag, which may be equipped with a safety valve set at 14 mm. of mercury as advocated by Waters.[2] A manual bellows respirator[3] with a safety valve that prevents excessive pressure is another means for giving intermittent positive pressure,[4] and a device of this sort has been accepted by the Council on Physical Medicine.[5] More recently another type of manual respirator (suck and blow) has been accepted[6]

TABLE 1.—*Comparison of Types of Apparatus*

Each of the seven types of apparatus compared in this report is identified by a number so as not to indicate the manufacturer; a list of the chief characteristics and a brief description of each type is given.

Type	Chief Characteristics	Description
1	Pressure-sensitive air-balanced valve	A gas-driven automatic device which administers intermittent positive pressure, the interruption being determined by a pressure-sensitive air-balanced valve. It is known also as pneumatic balance resuscitator (P. B. R.)
2	Pressure-sensitive spring-loaded valve	A gas-driven automatic device which administers intermittent positive pressure, the interruptions being determined by a pressure-sensitive spring-loaded valve
3	Flow-sensitive "Aviation Model"	A gas-driven device which administers intermittent positive pressure, the interruptions being determined by a flow-sensitive valve. It is known also as "Aviation Model"
4	Flow-sensitive "Research Model"	A gas-driven device, similar to type 3 but having in addition many adjustable features that make it versatile for scientific investigations; it is known therefore as "Research Model"
5	"Suck and blow"	A gas-driven device in which positive pressures alternate with negative (subatmospheric). The mechanism consists of a spring-loaded pressure-sensitive valve and in addition a Venturi device for producing suction
6	Hand-operated: slow	A hand-operated device in which positive pressure is produced by compressing a bellows; it is provided with a safety valve opening at a fixed pressure
7	Hand-operated: fast	A hand-operated device similar to type 6 but provided with a safety valve permitting faster escape of air

which has a pressure range from plus 20 to minus 10 mm. of mercury. Automatic mechanical intermittent pressure respirators include the accepted[7] "suck and blow" type with pressures ranging from plus 14 mm. to minus 9 mm. of mercury. Another type studied recently, the pneumatic balance respirator[8] developed by the Army Air Corps, is small and compact in size and has been found simple in operation and effective in providing adequate artificial respiration.[9]

From the Department of Medicine, Columbia University, and the Chest and Medical Services of the First (Columbia University) Division, Bellevue Hospital.

This work was performed under contract with the Aero Medical Laboratory, Wright Field, Dayton, Ohio. Additional support was provided by the Commonwealth Fund and the Life Insurance Medical Research Fund.

1. Drinker, C. K.: Pulmonary Edema and Inflammation, Cambridge, Mass., Harvard University Press, 1943, p. 88.

2. Waters, R. M.: Simple Method for Performing Artificial Respiration, J. A. M. A. **122**: 339 (Oct. 30) 1943.

3. The automatic and manual devices used to provide artificial respiration are commonly referred to as resuscitators. We shall refer to them as respirators, as resuscitation implies more than maintenance of respiration.

4. Kreiselman, J.: New Resuscitation Apparatus, Anesthesiology **4**: 498 (Nov.) 1943.

5. Kreiselman Resuscitator Bellows Type, Model 110, Acceptable, report of Council on Physical Medicine, J. A. M. A. **120**: 99 (Sept. 9) 1942.

6. Lung-ventilator Acceptable, report of Council on Physical Medicine, J. A. M. A. **121**: 1039 (July 31) 1943.

7. E. & J. Resuscitator and Inhalator Acceptable, report of Council on Physical Medicine, J. A. M. A. **112**: 1943 (May 13) 1939. Emerson Resuscitator Hospital and Portable Models Acceptable, report of Council on Physical Medicine, ibid. **119**: 414 (May 20) 1942.

8. Burns, H. L.: Pneumatic Balance Resuscitator, Air Surgeon's Bull. **2**: 306 (Sept.) 1943.

9. Motley, H. L.; Cournand, A.; Eckman, M., and Richards, D. W., Jr.: Physiological Studies on Man with Pneumatic Balance Resuscitator, "Burns Model," J. Aviation Med. **17**: 451 (Oct.) 1946.

A survey of the literature shows a lack of experimental physiologic data reported on man in condemnation or in support of the various respirator devices, with the exception of the one report given on the pneumatic balance type. The design of respirator apparatus for use on man has been based largely on data obtained on animals with respect to (*a*) the upper limit of pressure that could be used safely, (*b*) the beneficial effect of the "suck and blow" type on the circulation as claimed by some [10] and denied by others [11] and (*c*) the absence of pulmonary damage produced by intermittent pressure breathing with and without the negative phase.[12]

The curve of pressure of inspired air, registered at the mask, differs with different forms of respirator apparatus. There has been up to the present time little information on the quantitative effects of these various forms of artificial respiration on the circulatory dynamics in man. Therefore it seemed desirable to obtain direct physiologic measurements by making use of recent technics, including right heart catheterization,[13] on the pulmonic and systemic circulation in man

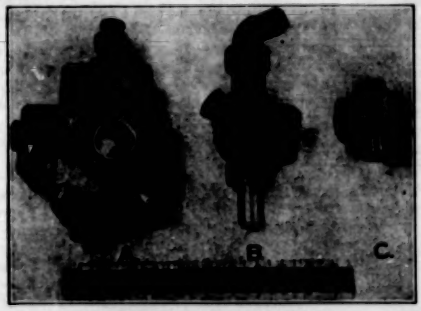


Fig. 1.—Automatic respirators: *A*, clinical research model, type 4; *B*, "Aviation Model," type 3; *C*, type 1.

when various types of respirators were used producing either intermittent positive pressure alone or combined with negative pressure during part of the cycle. In the present study physiologic and clinical observations have been made with various types of intermittent pressure respirators on 79 subjects. The data have been analyzed to determine the physiologic requirements of an ideal respirator, one which would provide adequate pulmonary ventilation with a minimal disturbance to the circulation. In addition the efficiencies of several respirators have been compared with manual methods, such as the Schaefer, for producing pulmonary ventilation in the type of subject who needs artificial respiration.

10. Birnbaum, G. L., and Thompson, S. A.: The Mechanism of Asphyxial Resuscitation, Surg., Gynec. & Obst. 75:79 (July) 1942.

11. (*a*) Volpitto, P. P.; Woodbury, R. A., and Abreu, B. E.: Influence of Different Forms of Mechanical Artificial Respiration, J. A. M. A. 126:1066 (Dec. 23) 1944. (*b*) Schwerma, H., and Ivy, A. C.: Safety of Modern Alternating Positive and Negative Pressure Resuscitators, ibid. 126:1256 (Dec. 29) 1945.

12. Orth, O. S.; Wilhelm, R. L., and Waters, R. M.: The Question of Pulmonary Damage with Artificial Respiration, J. Thoracic Surg. 14:230 (June) 1945. Schwerma and Ivy.[11b]

13. (*a*) Cournand, A., and Ranges, H. A.: Catheterization of the Right Auricle in Man, Proc. Soc. Exper. Biol. & Med. 46:462 (March) 1941. (*b*) Cournand, A.; Riley, R. L.; Breed, E. S.; Baldwin, E. deF., and Richards, D. W., Jr.: Measurement of Cardiac Output in Man Using the Technique of Catheterization of the Right Auricle or Ventricle, J. Clin. Investigation 24:106 (Jan.) 1945. (*c*) Cournand, A.: Measurement of the Cardiac Output in Man Using the Right Heart Catheterization, Federation Proc. 4:207 (June) 1945. Cournand, A.; Lauson, H. D.; Bloomfield, R. A.; Breed, E. S., and Baldwin E. deF.: Recording of Right Heart Pressures in Man, Proc. Soc. Exper. Biol. & Med. 53:34 (Jan.) 1944.

DESCRIPTION OF THE VARIOUS TYPES OF RESPIRATOR STUDIED

Type 1: Pressure-Sensitive, Air-Balanced Valve ("P.B.R.").—The first of the New Army Air Force models, the pneumatic balance resuscitator, hereinafter referred to as type 1 (fig. 1C) has been described and studied previously.[9] In the present study further observations have been made for comparison with other respirators. Type 1 is based primarily on pressure characteristics for actuating the pneumatic balance alternating mechanism. This mechanism automatically converts continuous positive pressure supplied by a pressure tank with a pressure-regulating valve into intermittent positive pressure. Inflation of the lungs occurs under positive pressure transmitted through a

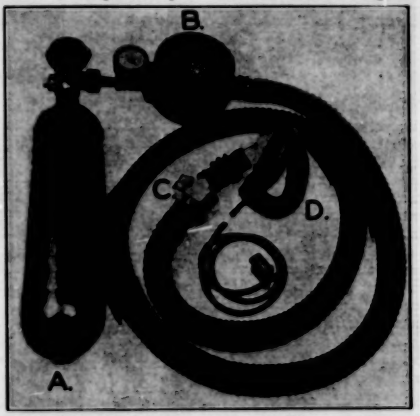


Fig. 2.—Small portable respirator outfit: *A*, high pressure oxygen cylinder; *B*, Bendix pressure demand regulator; *C*, type 1 respirator, and *D*, experimental face mask.

mask to the lungs, and after reversal passive deflation takes place almost to atmospheric pressure aided by the elasticity of the lungs and thoracic structures. The maximal pressure in the face mask is approximately 75 per cent of the continuous positive pressure or line pressure delivered by the regulating valve on the pressure tank, while the minimal pressure is about 10 per cent.[9] The Army Air Force's pressure-demand regulator, which supplies oxygen at atmospheric pressure during inspiration or maintains a continuous positive pressure adjustable up to 30 cm. of water by means of a regulator dial (fig. 2), provided a convenient means for maintaining a constant line pressure. The complete respirator unit can be assembled as a small, compact, portable outfit with a small oxygen cylinder, as shown in figure 2. The aluminum model respirator has been found simple to use, easy to maintain in operation and serviceable for long periods of time without special care.[9] A model made of plastic material was found to be unsatisfactory due to (1) warping of the disk supporting the rubber membranes and valve seat, resulting in a failure to cycle properly, and (2) the danger of breaking the fragile outside wall of the plastic case. All variables except line pressure regu-

lation are built in the device as fixed adjustments. There are no springs. Two rubber diaphragms constitute the only moving parts. Mask leaks greater than 10 per cent prevent proper cycling. The mask pressure curve obtained is symmetric with a constant upward slope during inspiration and constant downward slope during expiration (see fig. 3, II *A*). Inspiratory time is approximately equal to expiratory time.

Type 2: Pressure-Sensitive, Spring-Loaded Valve.—A small compact experimental automatic intermittent positive pressure respirator with a mechanism similar to that of type 5 without a Venturi device was tested. All adjustments are fixed on this model except frequency of alternation. The breathing pattern and mask pressure curves are similar to those of type 1 (fig. 3, II *B*). The maximal peak pressure on the model used was 15.1 mm. of mercury and the minimal was 2.2 mm. of mercury. In general the observations on this model were the same as for type 1. The discussion of the influence of type 1 on the respiration and circulation is also applicable for type 2 (for a comparable line pressure setting giving the fixed peak pressure of the latter).

Type 3: Flow-Sensitive, "Aviation Model."—The second new type developed by the Army Air Corps is shown in fig. 1 *B*[14] and hereinafter referred to as type 3. The principle of operation for this type is based primarily on flow characteristics for actuating the cycling mechanism. This model was designed for use with a compensated pressure valve used in the Army Air Forces A 13 and A 15 pressure demand oxygen masks. Expiration occurs more rapidly than with type 1, and the flow capacity is greater. The respirator mechanism reverses when the flow of gas through the cycling vane completely stops, a feature which requires that the mask fit on the face without leaks. The minimal pressure on expiration is 2.5 cm. of water and is unrelated to line pressure, while the maximal pressure is approximately the same as the line pressure. The flow sensitivity characteristic of the cycling mechanism is in contrast to type 1, which is primarily pressure sensitive. The mask pressure curve of type 3 is asymmetric, showing a gradual increase in pressure during inspiration and a sudden drop in pressure at the beginning of expiration, with the rest of the curve being concave upward until it levels off at a pressure of 2.5 cm. of water (fig. 3, I *D*). Inspiratory time usually exceeds expiratory time, but the ratio of inspiratory to expiratory time, the cycling rate and the ventilation can be varied widely.

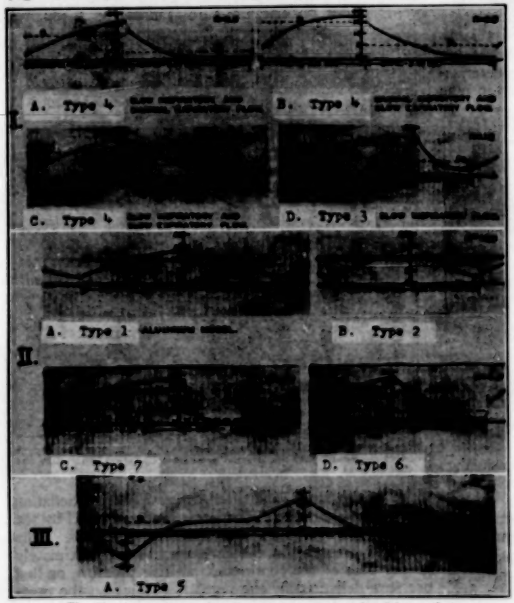


Fig. 3.—Various types of mask pressure curves produced by respirators (electric recording): Pi, inspiratory mean mask pressure; Pe, expiratory mean mask pressure. All pressures are recorded in millimeters of mercury.

Type 4: Flow-Sensitive, "Research Model"—A third type, newly developed by the Army Air Corps (fig. 1*A*),[13] is herinafter referred to as type 4. This instrument was designed to permit a study of more variables involved in intermittent pressure breathing than was possible with type 3. With type 4 the following can be varied separately or in various combinations: (*a*) line pressure, (*b*) inspiratory cycling rate, (*c*) expiratory cycling rate, (*d*) inspiratory flow rate, (*e*) expiratory flow rate and (*f*) expiratory pressure. Type 4 works automatically, and its characteristic alterations are determined by flow-time relationship provided by a separate cycling piston in the mechanism. It is stated that the cycling of the respirator is more positive than with type 3. Large mask leaks are tolerated without interfering with the cycling, due to the enclosure in the mechanism of a separate flow circuit acting on the cycling piston. (For a more detailed description consult article by Motley and others.[15] Type 4 does not require a Linde compensated pressure valve and may be used with any pressure face-mask or anesthesia-mask with an inflatable cuff. The mask pressure curve of type 4 is somewhat similar to that of type 3, characterized by the rapid initial drop in pressure at the beginning of expiration that progressively decreases to atmospheric. The variability in the type of tracing that can be obtained is much greater than with type 3 (fig. 4.; 1A, B and C). A slow inspiratory and maximal expiratory flow rate-setting produces a mask pres-

14. Carlson, L. D.: Design of an Intermittent Pressure Valve Obtained from V. Ray Bennett Through the University of Southern California, Memorandum Report, TSEAL 3-660-49-M, AAF Headquarters ATSC, Engineering Division Aero-Medical Laboratory, Wright Field, July 12, 1948.

15. Motley, H. L.; Cournand, A.; Werko, L.; Himmelstein, A.; Dresdale, D.; Johnson R.; Lester, M.; Spicrto, B., and Richards, D. W., Jr.: Physiological and Clinical Studies of Intermittent Pressure Respirators and Manual Methods for Producing Artificial Respiration in Man: Memorandum Report, TSEAA 696-79-P, AAF Headquarters A. M. C. Engineering Division, Aero-Medical Laboratory, Wright Field, Sept. 6, 1946.

sure tracing that has a gradual increasing pressure until a peak is reached, where cycling occurs and the pressure then drops rapidly to atmospheric (fig. 3, I *A*). The aforementioned respirator setting for flow rates results in maximal peak pressures with the lowest mean mask pressure for the entire cycle (see fig. 3, I *A*, *B* and *C*). Adjusting the expiratory flow rate to minimal instead of maximal as in the preceding combination results in a type 1 curve (fig. 3, I *C*). The transmission of line pressure in type 4 as peak mask pressure varies with the rate of inspiratory flow, approaching 100 per cent on a maximal inspiratory flow setting. When the inspiratory time tends to be longer than expiratory time, an unnecessarily high mean mask pressure for the entire cycle results.

Type 5: "Suck and Blow."—Type 5,[7] used as an example of the "suck-and-blow" type, has a negative pressure at the beginning of inspiration, which gradually becomes positive up to a certain peak pressure where reversal occurs. During expiration the pressure decreases gradually back to the starting point (fig. 3, III *A*); there are no variables to adjust in this model, as inspiration stops at a fixed positive mask pressure (plus 13.5 mm. of mercury) and expiration at a fixed

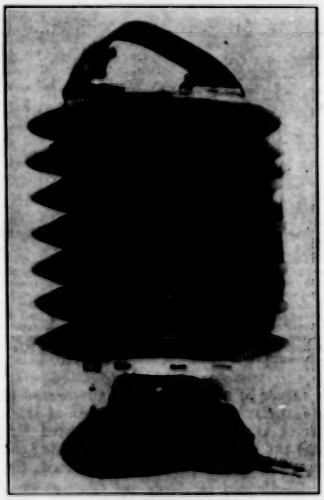


Fig. 4.—Type 7, hand-operated, fast: safety device permits faster escape of air than in type 6.

negative pressure (minus 11.1 mm. of mercury). The valves are spring-loaded, and a Venturi device which operates only during expiration provides the suction. With the model used, 37 per cent of the expiratory volume was added by use of the Venturi device. Inspiratory time is longer than expiratory time, and the cycling rate (i. e., frequency per minute) is slower than on the other respirators.

Type 6: Hand-Operated, Slow.—Type 6[8] is equipped with a safety valve which opens when the positive pressure reaches 17.5 mm. of mercury on the model used (fig. 3, II *D*). Positive pressure is produced by compressing a bellows, which builds up the pressure rapidly to a peak. When the valve opens expiration takes place rapidly and the mask pressure drops to atmospheric. Inspiratory and expiratory time may be varied by the operator. The maximal volume change for one stroke on the bellows measured 1,500 cc. The sliding valve arrangement of type 6 is rather awkward, as inexperienced operators may prevent effective ventilation with the device by blocking the valve by their hand.

Type 7: Hand-Operated, Fast.—Another model, type 7 (fig. 4), a bellows type, hand-operated respirator somewhat similar to type 6 was also studied. This model has also a safety valve that opens when the positive pressure reaches 17.5 mm. of mercury. The tracing of type 7 (fig. 3, II *C*) shows a gradually increasing mask pressure and then a rapid drop to atmospheric after expiration starts. The expiratory pressure drops to atmospheric more rapidly on type 7 than on type 6 (fig. 3, II *C* and *D*). The maximal volume change for one stroke on the bellows measured

Fig. 5.—Cardiac catheter with the tip in the right ventricle.

2,000 cc. The bellows and valve operation on type 7 was smoother and more foolproof than that on type 6. Inspiratory and expiratory time may be varied by the operator.

METHOD OF STUDY

Pulmonary ventilation was measured and compared with the various types of respirators, both automatic and manual in both conscious and unconscious subjects, using a Tissot spirometer or a portable recording spirometer. In cases of complete apnea the respirators were compared with manual methods for producing pulmonary ventilation. The position of the apneic subject was studied with particular reference to respiratory resistance and the influence on the resulting ventilation.

Respiratory gas exchange was determined by analysis on the Haldane apparatus for carbon dioxide and oxygen content of expired air collected in a spirometer. Also, samples of arterial blood from the brachial or femoral artery were analyzed for oxygen content and capacity and carbon dioxide content on the Van Slyke-Neill apparatus. The p_H was determined directly by use of a glass electrode; the oxygen saturation and pCO_2 (carbon dioxide concentration expressed in terms of pressure) were calculated. In 26 cases a total of

one hundred and two simultaneous samples of blood were obtained from the artery through an indwelling needle and from the right ventricle by means of a cardiac catheter introduced through the median basilic vein into the right ventricle (fig. 5), using a technic which has been described and discussed elsewhere.[16] The cardiac output was calculated by applying the Fick formula, using the data obtained from the samples of expired air, of mixed venous blood from the right ventricle and of arterial blood all collected simultaneously:

$$B = \frac{C}{D}$$

where B = cardiac output in liters per minute,
C = oxygen intake in cubic centimeters per minute and
D = difference in oxygen content between arterial and venous blood, in terms of cubic centimeters of oxygen per liter of blood.

(Example: Oxygen intake 200 cc. per minute with an oxygen arteriovenous difference of 40 cc. per liter of blood. Cardiac output = 5 liters per minute.)

Several measurements of cardiac output were obtained at intervals over a period of two to three hours. The subject had been maintained in a fasting state for the preceding sixteen hours. After introduction of the cardiac catheter and intra-arterial needle, a thirty minute rest period with the patient lying supine was used before the first measurement was taken while breathing air at ambient (prevailing atmospheric) pressure. The second cardiac output measurement was taken after ten to twenty minutes on a respirator, followed by a third measurement at ambient pressure in ten to twenty minutes. A fourth measurement was generally taken using either another type of respirator or the same respirator on a different line pressure. In a few cases a fifth measurement was taken either with another type of respirator or during spontaneous breathing. The patients were unanesthetized except for a small amount of procaine hydrochloride used in the skin where the needle and catheter were introduced.

Pressure recordings were obtained simultaneously from the brachial or femoral artery, the right ventricle, the mask pressure and, in 4 subjects having a therapeutic pneumothorax, from the pleural space. The Hamilton manometer for multiple pressure recordings[17] or the Clark pressure pick-up capsule with electrical amplification and recording were used.[18] Tracings were obtained from the same subject in three instances with both the Hamilton and the electrical methods of recording, separately and simultaneously. The pressures measured by the two systems checked closely. A simultaneous electrocardiogram was also obtained with the aforesaid recordings. The zero reference plane for cardiac pressure was taken 5 cm. below the angle of Louis, while the reference plane for arterial pressure was the level of the artery used. Systolic and diastolic pressures were calculated from the calibration curves and mean pressure by planimetric integration of the area under the curve for each pressure tracing.

16. (a) Cournand, A.; Riley, R. L.; Bradley, S. E.; Breed, E. S.; Noble, R. P.; Lauson, H. D.; Gregersen, M. I., and Richards, D. W., Jr.: Studies on the Circulation in Clinical Shock, Surgery **13**: 964 (June) 1943. (b) Cournand, A.; Bloomfield, R. A.; Lauson, H. D.: Double Lumen Catheter for Intravenous and Intra-Cardiac Blood Sampling and Pressure Recording, Proc. Soc. Exper. Biol. & Med. **60**: 73 (Oct.) 1945. (c) Cournand, Riley, Breed, Baldwin and Richards.[5b]

17. Richards, D. W., Jr., and Cournand, A.: Final Report of Work Under Contract OEMcmr 107, from March 1, 1942 to Nov. 30, 1945.

18. Motley, H. Ia.; Cournand, A.; Werko, L.; Dresdale, D.; Himmelstein, A., and Richards, D. W., Jr.: Intravascular and Intracardiac Pressure Recording in Man: An Electrical Apparatus Compared with the Hamilton Manometer, Proc. Soc. Exper. Biol. & Med. **64**: 241 (Feb.) 1947.

A simulated breathing device was used to test the mechanical features of the various respirators. This set-up consisted of a G 1 low pressure oxygen cylinder (internal volume 34,419 cc.) with a 500 cc. special type mask breathing bag connected on one end. The tidal volume approximates that of man, and the device provides both the distensibility and retractability factors present in the lungs.

MATERIAL FOR STUDY

The cases studied in this paper may be divided into four main groups, (1) essentially normal trained volunteers, (2) unanesthetized conscious subjects studied by cardiac catheterization, (3) patients in deep coma and (4) patients in complete apnea. The observations and measurements for each group are given in table 2.

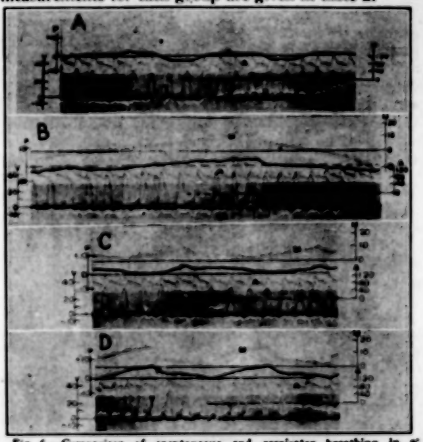


Fig. 6.—Comparison of spontaneous and respirator breathing in a subject with essentially normal circulation: *A*, pressure tracing during spontaneous (ambient) breathing; from above downward—pleura, brachial artery and right ventricle; *B*, pressure tracings while breathing with type 5; from above downward—mask, pleura, brachial artery and right ventricle; *C*, pressure tracings while breathing with type 1, same order as in *B*; *D*, pressure tracings while breathing with type 4, same order as in *B*. On the tracings: V_r, right ventricle; A, brachial artery; P, pleura; M, mask; all pressures in millimeters of mercury.

RESULTS

A. *Influence of the Various Respirators on Ventilation and Gas Exchange.*—1. Comparison of Mask Pressure Curves Obtained with the Simulated Breathing Apparatus and in Conscious Subjects: Using the simulated breathing device previously described, the mask pressure curves were studied using the automatic respirators. These curves, illustrated in fig. 3, are identical to curves obtained on well relaxed subjects

TABLE 2.—*Material for Study and Observations Made*

Type of Case	No. of Subjects	Type of Observation
Normal trained volunteers	10	Pulmonary ventilation; air and blood gas exchange
Conscious subjects	36	Pleural pressure (4 cases); pulmonary ventilation; air and blood gas exchange; cardiac output; intracardiac and peripheral artery blood pressure recordings; mask pressure
(a) Essentially normal circulation	17	
(b) Arteriosclerotic heart disease	7	
(c) Shock from hemorrhage	2	
Deep coma	22	Pulmonary ventilation; air and blood gas exchange; clinical observations
Complete apnea	21	Pulmonary ventilation; imposed frequency pressures required; influence of position

and represent comparable ventilation volumes. In unrelaxed subjects deviations from the preceding type of curves frequently occurred. Failure of the inspiratory part of the curve to rise early in inspiration has been observed with all the automatic intermittent positive pressure respirators. This was due to a superimposed inspiratory effort on the part of the subject. The negative phase of the curve obtained with the type 5 respirator was often reduced in length and depth as the result of positive efforts by the patient to terminate the suction phase. Type 1 and also types 3 and 4 tended to follow the slightest breathing effort of conscious subjects, but with types 2 and 5 the subject had to follow the respirators to get proper ventilation.

2. Ventilation and Gas Exchange in Different Types of Subjects: (*a*) Conscious: Data from 47 experiments concerning the effect of the automatic respirators on ventilation and gas exchange in conscious subjects systematically studied, including cardiac catheterization, are given in table 3. The increase in pulmonary ventilation varied from 23.3 per cent with type 1 to 105 per cent with type 4. The ventilation rise was due to an increase

TABLE 3.—*Respirators Using Compressed Air*

Comparison of effects on pulmonary ventilation and the CO_2 content, pCO_2 and p_H of arterial blood

	Respirator Type			
	1: Pressure-Sensitive	3: Flow-Sensitive "Aviation Model"	4: Flow-Sensitive "Research Model"	5: "Suck and Blow"
Number of experiments	22	9	11	6
Mean mask pressure, Mm. Hg	+7.2	+9.8	+6.3	+3.0
Respiration rate				
Per minute	14.2	14.3	15.9	8.3
Per cent change *	−23.4	−22.0	−27.4	−56.6
Pulmonary ventilation				
Liters per minute	10.6	12.8	15.3	11.0
Per cent change *	+23.3	+47.1	+105.0	+47.0
Arterial blood				
O_2 saturation				
Per cent	96.5	98.7	98.4	96.7
Per cent change *	+2.7	+3.4	+2.3	+2.8
CO_2 content				
Volume per cent	47.1	46.9	47.6	52.5
Change in volume per cent *	−0.7	−4.2	−1.9	−2.5
pCO_2				
Mm. Hg	34.2	28.1	30.2	27.9
Change in mm. Hg *	−3.1	−12.6	−5.9	−6.3
p_H				
p_H	7.47	7.55	7.50	7.51
Change in p_H units *	+0.05	+0.12	+0.07	+0.07

* With respect to ambient (spontaneous breathing at atmospheric pressure).

in tidal volume, for the respiration rate was decreased from 21.4 per cent with type 4 to 56.6 per cent with type 5. In general there was a slight increase in the percentage of saturation of oxygen in the arterial blood (2 to 3 per cent, table 3). When the subjects were using the respirators with compressed air, the carbon dioxide content was decreased slightly with all the automatic respirators, varying from minus 0.7 volumes per cent with type 1 to minus 4.2 volume per cent with type 3.

The p_H increased from 0.05 units with type 1 to 0.12 units with type 3, and accordingly the calculated pCO_2 decreased by 3.1 and 12.6 mm. of mercury respectively. With the exception of type 4, there was a good correlation between the degree of hyperventilation caused by the various respirators and the extent of pCO_2 changes. This may have been due in type 4 to the greater dead space in the hose line connection of the mask to the respirator, which resulted in greater rebreathing than on the other models.

Changes in blood gases and p_H observed after the respirators were in use for several hours were of the same magnitude as the changes observed after ten to fifteen minutes. The respiratory alkalosis observed was of little clinical significance. Even in the patients using type 3, where the changes were most pronounced (pCO_2 25.2 mm. of mercury, p_H 7.58) no manifestation of tetany was observed. Observations after sixty minutes[9] at a 25,000 feet (7,620 meters) simulated altitude with subjects hyperventilating showed still lower pCO_2 and higher p_H without any evidence of tetany.

Observations on pulmonary ventilation and gas exchange in 10 essentially normal trained volunteers were similar to the data reported on the catheterized group in table 3.

(*b*) Deep coma: The automatic respirators were used on 22 patients in deep coma with respiratory difficulties. The diagnoses were as follows: 8 cerebrovascular accidents; 3 cardiac disease in terminal failure; 2 ethyl alcohol poisoning; 2 carbon monoxide poisoning; 2 barbiturate poisoning; 1 methyl alcohol poisoning; 1 immersion; 1 heat exhaustion and epilepsy; 1 irreversible hemorrhagic shock, and 1 pneumonia.

The automatic respirators produced adequate ventilation (5 to 18 liters per minute, average 10.5 liters per minute) in all types of unconscious subjects without adverse effects from hyperventilation. The following illustrative data were obtained in an instance of cerebrovascular accident, the patient in coma with Cheyne-Stokes breathing: On ambient air the ventilation varied from 8 to 40 liters per minute and in the arterial blood the pCO_2 was 34.9 mm. of mercury, the p_H 7.53 and the oxygen saturation 81 per cent. With type 1 on compressed air the breathing was regular with a ventilation rate of 16 liters per minute, pCO_2 37.8 mm. of mercury, p_H 7.47 and the oxygen saturation 93 per cent in the arterial blood. With type 1 on 100 per cent oxygen the breathing was regular with a ventilation rate of 17.5 liters per minute, pCO_2 36.0 mm. of mercury, p_H 7.49 and the oxygen saturation 102 per cent. The line pressure used above was 21 cm. of water (15.4 mm. of mercury for type 1 on both compressed air and 100 per cent oxygen. On ambient 100 per cent oxygen, following the use of type 1, the breathing remained regular with a ventilation of 14 liters per minute, pCO_2 38.5 mm. of mercury, p_H 7.46 and the oxygen saturation 105 per cent in the arterial blood. When the patient was changed to air, the Cheyne-Stokes breathing reappeared in two minutes.

In patients with a gasping type of inspiration there was a very high instantaneous flow rate of short duration (0.4 to 0.6 second) with maximal peak flows during this interval up to 80 to 120 liters per minute.[13] Type 4 flow-sensitive "Research Model" was the only respirator with sufficient instantaneous flow capacity to eliminate the negative phase at the beginning of inspiration due to additional inspiratory effort.

Usually the respirators were used with a mask, but in 2 cases type 1 and type 4 were used attached to an endotracheal tube. Lower regulator line pressures give adequate ventilation with an endotracheal tube as compared to the line pressures required when using the mask.

Type 1, Pressure-sensitive pneumatic balance resuscitator, was the only automatic respirator considered safe enough in the mechanical operation and sufficiently innocuous in its physiologic effects to be left with a minimum of ward supervision on patients in coma for extended periods of time, one to two days or longer if necessary. Type 1 has been used up to seventy-nine hours continuously in the treatment of a patient with barbiturate poisoning without demonstrable ill effects, either clinical or pathologic.

(c) Complete apnea: It has been pointed out that the fresh cadaver much more closely simulates the completely apneic living subject than does the normal conscious person.[19] Therefore, observations have been made on 18 subjects at or shortly after the time of death, in addition to 3 living subjects with complete apnea. Adequate pulmonary ventilation was obtained with all the respirators provided the subject was in the proper position, except in 1 case. The subject in the aforementioned case had bulbar palsy with dysphagia and had died as the result of a complete blocking of the upper trachea with solid particles of food. The onset of rigor mortis has been the factor limiting the length of time that type 1 will ventilate the lungs after death.[9] The preceding factor also holds for all the other types, both automatic and hand-operated respirators. The best position of the body has been discussed for type 1.[9] This body position consists in hyperextension of the head on the cervical vertebrae (push the head back) with support of the lower chin and a slight Trendelenburg position. This position was found to be the best for all respirators, both automatic and hand-operated, and was in most instances the determining factor between success or failure for proper performance of the automatic respirators in apneic subjects.

The frequency of alternation and the pulmonary ventilation produced by the various automatic respirators are shown in table 4. Line pressures used to ventilate the lungs averaged 15.8 mm. of mercury for type 1, 13.6 for type 3, and 12.0 for type 4. Types 2 and 5 have fixed line pressures. The line pressure with type 1 had to be increased approximately 25 per cent over those of types 3 and 4 in order to get the same peak mask pressure, due to less transmission of line pressure in type 1. All the automatic respirators which were tested gave adequate pulmonary ventilation with a mask if the line pressure was 11.8 mm. of mercury (16 cm. of water) or higher. The values for types 3 and 4 were obtained with the adjustments set for medium inspiratory flow and alternating frequency. By increasing the inspiratory flow and the alternating frequency on types 3 and 4 the total pulmonary ventilation could easily be increased on each of the different line pressures used. Types 3 and 4 were slightly more capable of overcoming breathing resistance in the upper part of the pharynx and maintaining proper alternation frequency than the others. In order to prevent types 3 and 4 from ventilating the lungs a complete blockage of the airway must be present, as the design of the apparatus is based on flow sensitivity. Type 1 tolerates airway obstruction slightly better than type 5. Type 2 responds in the same manner as type 1.

Both manual respirators (types 6 and 7) provided adequate ventilation in the apneic subjects tested. The operator controlled the frequency of alternation. The respiratory excursions produced by the manual respirators were preponderantly diaphragmatic in character; this was also true for the automatic respirators. Although the exact ventilation volume was not measured with the manual models, the amount was considered adequate as judged by the abdominal excursions and breath sounds, and these correspond with observations made on the same subjects with the automatic respirators in cases in which an adequate ventilation volume was measured.

In contrast to the adequate pulmonary ventilation secured with the various respirators, manual methods used on the same test subject were grossly inadequate. Observations were made on 4 suitable test subjects (cadavers), selected because they were known to have had clear lungs just prior to death. With the best positions of the body in the first case, the average tidal volume obtained with the Schaefer method was only 78 cc., and when the best position was not used no ventilation resulted. Type 1 easily ventilated this subject at a rate of 6 to 10 liters per minute, depending on the line pressure. In the second case with the best body position an average tidal volume of 50 cc. was secured with the Schaefer method. When the Schaefer method was used without hyperextending the head on the neck and supporting the lower jaw, ventilation did not result.

The two hand-operated respirators, types 6 and 7, ventilated the second subject adequately and with ease; respiratory movements were pronounced, and breath sounds were normal in character. All the automatic respirators ventilated this second subject adequately and with ease. In the third case with the Schaefer method an average tidal volume of 140 cc. was secured with the best position, and without hyperextension of the neck but with support of the lower jaw the tidal volume was reduced to 90 cc. Without hyperextension of the head and without supporting the lower jaw no ventilation resulted. This subject was easily ventilated with the automatic respirators at a rate of 6 to 10 liters per minute. In the fourth case the Schaefer method failed to ventilate the lungs even after the best position was secured. The Eve (rocking) method gave 50 to 60 cc. per tidal volume with the best position of the head. If the head were not held properly no ventilation could be measured with the Eve method. The automatic respirators ventilated the fourth subject easily at a rate of 5 to 11 liters per minute depending on the setting of the various respirators and the line pressure used. Tests made with and without an airway tube in these 4 cases revealed no difference in the pulmonary ventilation.

In summary, in 4 apneic subjects even though great care was taken in testing the manual methods with the proper position of the body, head and lower jaw pulmonary ventilation was grossly inadequate, while adequate pulmonary ventilation was easily secured with the respirators; similar observations have previously been reported on comparing type 1 to the manual squeeze procedure as commonly carried out on a hospital bed.[9] Other studies have been reported on the inadequacy of the Schaefer method in the type of subject in need of artificial respiration.[19] The proper position for the head, lower chin and body, previously described,[9] was found to be the most advantageous for administering artificial respiration in apneic subjects either by respirator or manual methods.

Type 1 was used for ten hours to maintain artificial respiration in 1 case of methyl alcohol poisoning with complete apnea. With a line pressure of 21 cm. of water (15.4 mm. of mercury) the pulmonary ventilation averaged 6 to 8 liters per minute. At intervals type 1 was stopped, but no spontaneous respirations occurred. The mean blood pressure was low, maintained at 25 to 30 mm. of mercury in the femoral artery during the entire period. When sodium bicarbonate was given to correct the extremely low arterial blood p_H of 6.81, the

19. Comroe, J. H., Jr. and Drinker, R. D.: Artificial Respiration, J. A. M. A. 130: 381 (Feb. 16) 1946. Brauer, O.: Ueber Wiederbelebung Durch Künstliche Atmung, Klin. Wchnschr. 6: 1548 (Aug. 13) 1927. Cordier, D. G.: Methods of Artificial Respiration, Brit. M. J. 2: 381 (Sept. 25) 1943. Macintosh, R. R., and Mushin, W. W.: Pulmonary Exchange During Artificial Respiration, ibid. 1: 908 (June 15) 1946.

arterial pulse and blood pressure improved slightly with type 1 breathing as the p_H was raised to 7.30. Although the subject was decidedly cyanotic before using the respirator, shortly after starting type 1 the arterial blood was 100 per cent saturated. In this subject when type 1 was changed from 100 per cent oxygen to compressed air on the same line pressure the pulse became weak

TABLE 4.—*Alternation Frequency and Pulmonary Ventilation Produced with Various Respirators in Eighteen Patients with Complete Apnea*

Average Line Pressure			Number of Tests	Average Alternation Frequency per Min.	Average Pulmonary Ventilation L./Min.
Cm. H_2O	Mm. Hg	Respirator Type			
30	22.0	1: Pressure-sensitive	4	29	9.9
26	19.1	1: Pressure-sensitive	6	30	9.5
26	19.1	3: Flow-sensitive	3	27	10.2
21	15.4	1: Pressure-sensitive	9	22	9.3
21	15.4	3: Flow-sensitive	7	21	7.7
21	15.4	4: Flow-sensitive	3	14	10.3
16	11.8	1: Pressure-sensitive	8	35	7.9
16	11.8	3: Flow-sensitive	6	20	5.6
16	11.8	4: Flow-sensitive	4	24	8.0
12	8.8	1: Pressure-sensitive	1	60	9.0
12	8.8	3: Flow-sensitive	4	21	3.3
12	8.8	4: Flow-sensitive	3	23	6.3
		Average: All Line Pressures			
21.6	15.8	1: Pressure-sensitive	28	26	9.0
18.5	13.6	3: Flow-sensitive	20	22	6.6
16.3	12.0	4: Flow-sensitive	13	21	8.1
....	....	5: "Suck and blow"	4	12	8.2*

* Corrected volume (amount added by Venturi suction device has been deducted).

and the heart sounds faint. When 100 per cent oxygen was resumed with type 1 the improvement was immediate. During a routine lumbar puncture for examination of the cerebrospinal fluid the pressure was observed to fluctuate with the respirator cycling, with peak increases that represented 25 per cent of the peak mask pressure (16 cm. of water) on type 1. After ten hours the heart gradually failed and finally stopped. There was no urinary output during the ten hour period. Postmortem examination revealed extensive injury to the liver and kidneys as a result of the methyl alcohol poisoning.

Type 1 was used on 1 case of immersion, in which complete apnea developed shortly after the patient was brought into the hospital. There was pronounced cyanosis, a mottled purplish discoloration of the skin, white frothy fluid exuding from the mouth and acute pulmonary edema. The rectal temperature was 95 F. The condition was the result of immersion in sea water (East River, near Bellevue Hospital) while the patient was in a drunken stupor. Type 1 was used on a line pressure of 21 cm. of water with 100 per cent oxygen, and it maintained adequate ventilation. The cyanosis cleared after ten minutes, but about thirty minutes elapsed before the discoloration of the skin completely disappeared. After sixty minutes on type 1 the chest was clear anteriorly, with only a few moist rales left at the bases of the lungs posteriorly. Semiconsciousness returned after thirty minutes, and use of the type 1 respirator was discontinued after two hours. The patient made an uneventful recovery without contracting bronchopneumonia.

Type 1 was used on 1 adult man with acute anterior poliomyelitis complicated by a complete respiratory paralysis at Willard Parker Hospital, New York. This subject quickly became cyanotic when the Drinker type respirator was stopped, and manual methods applied by experienced operators were inadequate to prevent cyanosis from developing. On a line pressure of 21 cm. of water, adequate pulmonary ventilation was secured as judged by the subjective sensation of the patient, color of the skin and respiratory excursions of the chest and abdomen. Type 1 was used to permit nursing care and physical therapy while the respirator was stopped. Also, the subject was moved with ease from one building to another without discomfort. The face mask (fig. 2) was the most comfortable for this patient. The oxygen was too dry for continued use with type 1 without using a humidifier, as he complained of a dry throat and interference with swallowing. When the subject was changed to the respirator after being on 100 per cent oxygen with type 1 he complained of air hunger for a few minutes, but this sensation rapidly disappeared.

B. *Influence of the Various Respirators on the Circulation.*—In the 26 patients studied by means of cardiac catheterization, the records obtained permitted careful analysis of the effects on the circulation produced by increasing and decreasing mask pressures.

1. Heart Rate: The observations regarding heart rate made in 36 experiments on 24 subjects (17 with essentially normal circulation and 7 with cardiac disease) appear in table 5. The changes in heart rate during inspiration are listed separately and correlated with the corresponding mean mask pressure. Increase in heart

TABLE 5.—*Heart Rate and Mean Mask Pressure During Inspiration and Expiration with Various Types of Respirators*

		Inspiration			Expiration		
		Mean Mask	Heart Rate		Mean Mask	Heart Rate	
Respirator Type	Number of Experiments	Pressure, Mm. Hg	Per Min.	Per Cent Change from Ambient	Pressure, Mm. Hg	Per Min.	Per Cent Change from Ambient
1: Pressure-sensitive	11	6.4	90	+9.0	6.0	90.0	+3.0
3: Flow-sensitive "Aviation Model"	8	12.4	86	+17.0	7.2	79.0	+7.0
4: Flow-sensitive "Research Model"	11	9.0	80.6	+4.1	1.9	83.5	−0.7
5: "Suck and blow"	6	5.1	81.7	−1.7	0.5	86.5	−0.8

rate during the period of increasing pressures was more appreciable than during the period of decreasing pressure with type 1, type 3 and type 4. During the period of increasing pressure with an average mean mask pressure of 9.3 mm. of mercury for the three respirators just mentioned, the average increase in heart rate was approximately 10 per cent; during the period of decreasing pressure, with an average mean mask pressure of 5.1 mm. of mercury, the average increase in heart rate was approximately 4 per cent. With type 4 the change in heart rate was insignificant during the expiratory phase, which is characterized by a rapid drop in pressure approaching zero with a low mean mask pressure. There was no essential change in heart rate during the period of increasing and decreasing pressure while breathing on type 5, as shown in table 5. This was probably related to the low mean mask pressure present during both inspiration and expiration.

2. Electrocardiogram: Significant electrocardiographic changes on lead 2 were not observed in the 26 subjects during intermittent positive pressure breathing. There was also no change in the time intervals between

the electrical and mechanical events in the right heart, as compared to the records of spontaneous breathing (fig. 6 and 7).

3. Blood Pressure. The influence of intermittent positive pressure on blood pressure was studied on 17

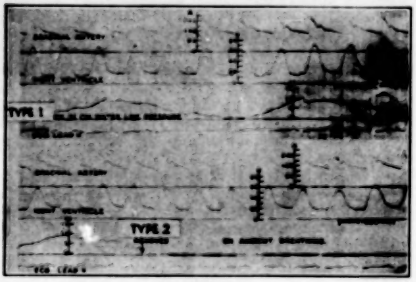


Fig. 7.—Pressure tracing in a case of essential hypertension. Electric recording was used in contrast to multiple simultaneous recordings with Hamilton manometer in previous figures: *A*, brachial artery pressure; *M*, mask pressure; *V*, right ventricle pressure. All pressures in millimeters of mercury on the scale.

subjects with an essentially normal circulation. The average arterial and right ventricular blood pressures during breathing with the four automatic respirators are given in table 6 with the corresponding mean mask pressures. Records illustrating simultaneous recordings of intra-arterial (femoral or brachial), intraventricular, pleural and mask pressures and electrocardiographic lead 2 are presented in figures 6, 7 and 8.

TABLE 6.—*Influence of Various Respirators on Blood Pressure and Peripheral Resistance in Subjects with Essentially Normal Circulation*

	Respirator Type			
	1	3	4	5
Number of experiments	13	7	7	6
Mean mask pressure, mm. Hg	7.7	10.1	8.1	2.6
Arterial blood pressure				
Systolic, mm. Hg	136	137	135	126
Change,* mm. Hg	+6	−3	+1	+9
Diastolic, mm. Hg	82	85	83	76
Change,* mm. Hg	+5	+2	+3	+9
Pulse pressure, mm. Hg	54	52	52	50
Change,* mm. Hg	+1	−5	−1	0
Mean, mm. Hg	100	106	102	95
Change,* mm. Hg	+3	+1	+3	+9
Right ventricular blood pressure				
Systolic, mm. Hg	28	30	31	28
Change,* mm. Hg	+1	+3	+3	0
Diastolic, mm. Hg	5.0	7.9	5.2	4.6
Change,* mm. Hg	+2.6	+6.9	+2.9	+2.7
Pulse pressure, mm. Hg	23.0	22.1	27.8	23.4
Change,* mm. Hg	−1.6	−1.9	+2.1	−2.2
Mean, mm. Hg	12.8	13.8	13.5	11.6
Change,* mm. Hg	+1.1	+5.1	+3.9	+0.8
Peripheral resistance				
Dynes—sec. / Cm.$^{-5}$	1,132	1,150	1,430	1,112
Per cent change*	+21.8	+6.3	+12.8	+6.3

* With respect to values obtained during spontaneous breathing; actually, the procedure involved in most cases in sequence: (1) a period of spontaneous breathing; (2) a period of pressure breathing, and (3) a second period of spontaneous breathing. The second period was compared with the average of the first and third periods.

The changes in systolic, diastolic, pulse and mean pressures are of low magnitude with all the automatic respirators, as is seen in table 6. The arterial systolic pressure with type 3 breathing decreased 3 mm. of mercury in contrast to a slight increase with the other respirators; however, the mean mask pressure on the former was the highest. Right ventricle pressures were increased with respect to ambient subjects with type 3 and type 4, while with type 1 and type 5 the changes were minimal. The mean right ventricular pressure was increased from plus 0.8 mm. of mercury on type 5 to plus 3.9 mm. of mercury on type 4, somewhat correlated with the mean mask pressure.

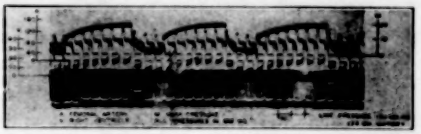


Fig. 8.—Pressure tracings while breathing with the type 3 (intermittent positive pressure) respirator: from above downward—mask, femoral artery and right ventricle.

4. Peripheral Vascular Resistance: The peripheral resistance was increased with all the automatic respirators (table 6). The calculation of peripheral resistance was made according to the formula [16a] generally in use with entries for the mean arterial blood pressure, the end diastolic right heart pressure and the cardiac output.

5. Cardiac Output: The effects of the four automatic respirators on the cardiac output in thirty-three experiments on 17 subjects with essentially normal circulation are presented in table 7. Type 1 with an average mean mask pressure of 7.7 mm. of mercury produced a

TABLE 7.—*Effects of Various Respirators on Breathing Characteristics of Cardiac Output in Subjects with Essentially Normal Circulation*

Respirator Type	Number of Experiments	Mean Mask Pressure, Mm. Hg	Mean Mask Pressure, % of Line Pressure	Frequency of cycles per Min.	Inspiratory Time, Sec.	Expiratory Time, Sec.	Ratio: Inspiratory to Expiratory	% Change in Cardiac Output with Respect to Output During Natural Breathing
1: Pressure-sensitive	13	+7.7	48.1	10.6	3.17	3.66	0.87	−10.8
3: Flow-sensitive	8	+9.8	59.7	11.3	3.06	2.68	1.18	−12.9
4: Flow-sensitive	7	+8.1	51.6	11.6	3.78	2.32	1.66	−5.9
5: "Suck and blow"	5	+2.6	....	6.9	7.31	3.61	2.07	+1.9

decrease in cardiac output of 10.8 per cent. This decrease was apparently proportional to the increase in mean mask pressure, as seen in figure 9, which is based on data obtained in thirteen experiments in subjects with essentially normal circulation. With a slightly higher mean mask pressure (8.1 mm. of mercury) the reduction in cardiac output with type 4 averaged only 5.9 per cent. With a mean mask pressure significantly higher, 9.8 mm. of mercury, the reduction in cardiac output with type 3 averaged 12.9 per cent. The mean mask pressure for type 5 was exceedingly low (2.6 mm. of mercury), and there was an insignificant change in cardiac output with respect to the values for natural breathing. An example of the different effect of type 1 and type 4 on the cardiac output in a subject under basal metabolic conditions who was studied repeatedly on the same day is given in table 8.

In ten experiments on 7 patients with arteriosclerotic heart disease no significant change (−2.0 per cent) in cardiac output was observed as a result of using the respirators on the following line pressures: the average

pressure with type 4 in four experiments was 11 mm. of mercury and with type 1 in six experiments, 14.7 mm. of mercury. The resulting mean mask pressures were low—the average with type 4 was 5.3 mm. of mercury and with type 1, 5.6 mm. of mercury.

The changes in cardiac output were insignificant in 2 instances of hemorrhagic shock when type 1 was used with a line pressure of 8.8 mm. of mercury (12 cm. of water).

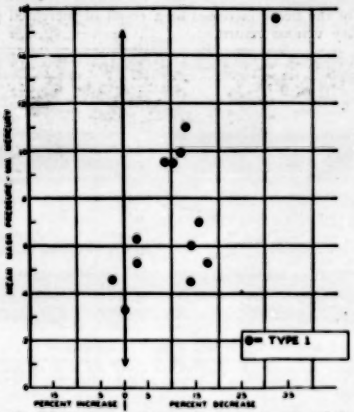


Fig. 9.—Relation between mean mask pressure increase and change in cardiac output from control ambient in patients with essentially normal circulation. Note the proportional decrease as the mean mask pressure increases.

Data were secured in 4 persons having a therapeutic pneumothorax by measuring pleural pressures simultaneously with the mask, right ventricle and arterial pressures. Information was thus obtained concerning the net filling pressure at the end of diastole in the right ventricle in relation to mask and pleural pressure variations. The right ventricular pressure changes were related to pleural rather than to mask pressure changes. In 2 subjects with structural changes in the lungs and in the pleura this relation was clearly demonstrated, as there was a lag of about one second between mask and pleural pressure changes. An analysis was made beat by beat of the heart, measuring simultaneously mask pressure, pleural pressure, right ventricular and arterial systolic and diastolic pressures and the right ventricle net filling pressure.[18] The net filling pressure, obtained by subtracting the simultaneously measured pleural pressure from the end diastolic pressure in the right ventricle, changed generally inversely with the pleural pressure. An increase in the net filling pressure corresponded to a decrease in pleural pressure. Successive decrease and increase in net filling pressure were therefore well in phase with variations in venous return to the right heart, which follow changes in intrathoracic pressure. An increase in the net filling pressure should result, according to Starling's law, in an increase in the output from the right heart, and a decrease should result in a decrease in output. During inspiration in intermittent positive pressure breathing, the increase in pleural pressure during inspiration results in a decrease in the net filling pressure of the right ventricle and therefore in a decreased output from the right heart. During expiration the pleural pressure decreases (rapidly or slowly depending on the type of mask pressure curve produced by the respirator), and this decrease results in an increase in the net filling pressure of the right ventricle, leading to an increase in cardiac output from the right heart.

Similar studies on the output of the right heart during normal deep breathing in man [20] have been interpreted as indicating an increase in right ventricle stroke volume during inspiration and a decrease during expiration.

In the 4 patients with pneumothorax the arterial pulse pressure curves were more or less parallel to the pleural pressure curves. In the case of M. W. (fig. 10, table 9), with a very long sustained increase in pleural pressure the arterial pulse pressure increased at first and then rapidly decreased, indicating a reduction in left heart stroke volume after a few beats. This result confirms previous studies made on sustained forceful expiration in man.[20] The latter change may be interpreted as indicating that after a short interval of time the effect of the reduction in right heart stroke volume was transmitted to the left heart, causing a diminution in left heart stroke volume and therefore a reduction in arterial pulse pressure. A similar change is shown in fig. 6 *B* with type 5.

The transmission of the negative phase with type 5 ("suck and blow") was very slight in the case of M. W. with a frequency of 14 cycles per minute (fig. 6 *B*). The negative pressure did not result in a striking increase in right ventricle net filling pressure, and the lowest filling pressure present corresponds to the lowest

TABLE 8.—*Comparison of Breathing Characteristics and Changes in Cardiac Output in One Subject Studied on the Same Day with Both the Type 1 and Type 4 Respirators*

	Respirator Type	
	1	4
Line pressure, mm. Hg	15.4	15.4
Mean mask pressure		
Inspiration, mm. Hg	6.0	10.9
Expiration, mm. Hg	4.5	2.3
Entire cycle, mm. Hg	5.2	6.9
Time		
Inspiratory time, sec.	2.19	2.28
Expiratory time, sec.	2.62	2.27
Ratio inspiratory to expiratory	1.21	1.00
Pulmonary ventilation		
Liter per minute	10.9	19.1
Per cent change from ventilation during natural breathing	+25.3	+120
Cardiac output		
Liter per minute	7.21	9.87
Per cent change from output during natural breathing	−17.5	+3.7

TABLE 9.—*Comparison of Unfavorable (A) and Favorable (B) Time Ratio for Mask Pressure on Cardiac Output with Type 4 Respirator*

	Line Pressure, Cm. Water	Ratio: Inspiration to Expiration	Cardiac Output		Mean Mask Pressure, Mm. Hg	
			Liter/Min.	Per Cent Decrease from Control Ambient	During Inspiration	During Expiration
A	20	3.9	3.7	39.0	16.8	3.8
B	16	0.9	6.0	1.0	7.9	2.0

[20] Lauson, H. D.; Bloomfield, R. A., and Cournand, A.: The Influence of Respiration on the Circulation in Man with Special Reference to Pressures in the Right Auricle, Right Ventricle, Femoral Artery and Peripheral Veins, Am. J. Med. 1: 315 (Oct.) 1946.

negative pressure of the mask. Also, the arterial pulse pressure on the same subject (M. W.) was not influenced by variations in mask pressure. No evidence was obtained that negative pressure during part of the cycle increases cardiac output. On the other hand, the "suck and blow" type respirator did not produce adverse effects on the circulation when used for one hour in 2 cases of deep coma. The negative mask pressure was transmitted much less to the pleural pressure than the positive pressure.

In summary, intermittent pressure breathing will result in the following cycle changes due to variations in intrathoracic pressure: (1) during the increasing inspiratory pressure period the venous return to the right heart diminishes; (2) during the phase of diminishing expiratory pressure the reverse takes place, and (3) the more rapid and complete the pressure drop to zero after reversal at the peak pressure, the greater the filling of the right side of the heart during expiration.

The over-all changes in cardiac output will vary with the type of pressure curve. Type 1 produces a symmetric type of curve, and the pressure drops slowly at approximately the same amount per time unit as the increase during inspiration. The time on low pressure during one complete cycle is about the same as the time on high pressure. The changes in cardiac output are more related to the height of the mean mask pressure

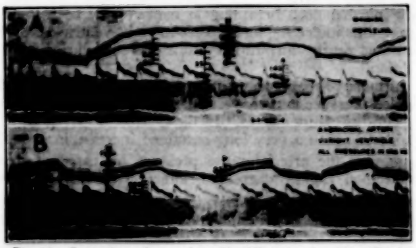


Fig. 10.—Comparison of an unfavorable (*A*) and a favorable (*B*) time ratio for mask pressure on cardiac output with the type 4 respirator (Hamilton manometer recording).

than to the ratios between inspiration and expiration. In the case of type 4 curve the rapid initial drop of pressure in expiration (fig. 11) allows the deficit occurring during the inspiration to be partly overcome in the first few beats. The complete compensation, however, will be dependent on two factors, (*a*) the duration of the expiratory period with as many heart beats as during inspiration and (*b*) the pressure existing during this time. The expiratory mean mask pressure on type 3 is relatively higher (2.5 cm. of water as a minimum) than on type 4. Hence type 3 occupies a position between type 1 and type 4 with respect to the decrease in cardiac output. In the case of type 4 the rapid drop in pressure and the total low expiratory mean mask pressures favor compensation of the deficit occurring during the inspiratory phase of rising pressures. A high mean mask pressure with type 4 results in large decreases in cardiac output (fig. 10 *A*), but to produce a high mean mask pressure for the entire cycle (12 to 15 mm. of mercury) with type 4, a short expiration time is required, thus not permitting adequate time for compensation to occur.

COMMENT

A. *Interpretation of the Mechanism of Action of Intermittent Pressure Breathing on the Circulation.*—It has been shown previously that in normal subjects the stroke volume of the two ventricles is unequal during deep breathing.[20] As the pressure in the thorax increases during expiration, filling of the right side of the heart from the large veins is reduced and the stroke volume diminishes; meanwhile, the output from the left side of the heart increases as a result of increased pulmonary venous return.

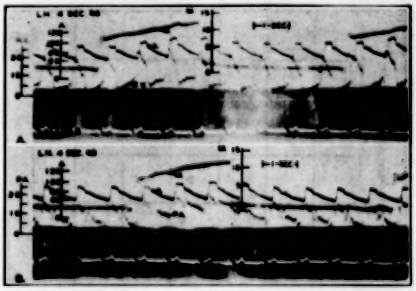


Fig. 11.—Desirable type of mask pressure curves produced by the type 4 respirator; there was no decrease in cardiac output; pressure tracings from above downward—*A*, mask, brachial artery and right ventricle; *B*, mask, brachial artery and pulmonary artery (Hamilton manometer recording).

The present study indicates that the same mechanism operates during intermittent pressure breathing in a reverse fashion and to a greater extent. The phase of rising intrathoracic pressure takes place during inspiration and the phase of decreasing pressure during expiration. The decrease in output from the right side of the heart, during the phase of rising pressure in the mask and in the thorax, is made up during the phase of falling mask pressure. For the left side of the heart the reverse occurs. However, the left side of the heart can only increase its output during inspiration for a short time (three to five beats) by ejection of blood squeezed out of the lungs. More extended increase in output of the left side of the heart will take place only after more blood has been supplied again by the right side of the heart. Thus, the variation in stroke volume of the right ventricle is the important part to consider in relation to sustained changes in cardiac output.

During intermittent pressure breathing the pressure should not only be low during expiration, but this phase of low pressure in the thorax should be of sufficient length. The total expiratory time interval should allow a sufficiently large number of heart beats to take place to compensate for the reduction in output which occurs during the inspiratory period of rising pressure. The type 1 symmetric curve (figs. 6 *C* and 3, II *A*) with inspiratory and expiratory time almost equal, affects the cardiac output through the entire cycle. There is positive pressure in the thorax during the whole of the respiratory cycle, which diminishes continuously the venous return of blood to the right side of the heart. The greater the increase in mean mask pressure, the larger the reduction in cardiac output with the type 1 respirator (fig. 9). The type 3 curve has a quick pressure drop on expiration, which permits the right side of the heart early in expiration to make up

part of the loss incurred during inspiration, but the compensation is not complete as the pressure does not return to atmospheric and the expiratory time interval is too short. In fig. 8 there are only approximately three heart beats during expiration with type 3 to make up for the decreased output of six heart beats during inspiration.

The type 4 curve also has a quick pressure drop on expiration and thus permits an early compensation. Complete compensation occurs in those subjects using type 4 in whom the expiratory time is long enough and the expiratory pressure is allowed to drop to atmospheric (fig. 11). In patients with short expiratory time intervals the compensation is incomplete (fig. 10 *A*). The decrease in cardiac output on type 5 is insignificant, as this respirator produces a mean mask pressure that is relatively low during the positive phase and only slightly above atmospheric for the entire cycle.

B. *Ideal Type of Respirator Equipment.*—The ideal type of respirator for use on man (producing effective artificial respiration with a minimal disturbance to the circulation) should embody the following characteristics:

1. It should be simple and sturdy in construction and operation, small and compact in size, as in type 1, type 2 and type 7. The respirator apparatus should stand steam sterilization if expiration occurs through part of the device as in type 1. Expiration should not occur through the flow-sensitive respirators with reversing pistons as in type 4.

2. The mask pressure curve should increase gradually during inspiration up to a peak not in excess of approximately 25 cm. of water, and after reversal occurs the pressure drop should decrease rapidly to a final pressure near atmospheric (figs. 11 and 3, I *A* and II *C*). The mean mask pressure during the expiratory period should be as low as possible. There is no apparent advantage of including negative pressure in the cycle.

3. Alternating frequency rates should maintain a respiratory rate between 10 and 20 per minute.

4. The volumes of pulmonary ventilation provided should be on an average from 6 to 10 liters per minute.

5. A regulator line pressure should be provided that takes into account the pressure drop in transmission for the particular type of respirator used and provides peak pressures from 10 to 25 cm. of water (7.4 to 18.4 mm. of mercury).

6. The mask most suitable for use in this study has been one having a wide, inflatable, thin, soft rubber cuff built over a sponge-type cushion base and detachable from a light weight transparent plastic facepiece (fig. 2 *D*). This type of mask has provided the best leakproof fit and the least dead space.

SUMMARY AND CONCLUSION

1. In this study all the automatic respirators tested produced adequate ventilation in all types of subjects, whether conscious, comatose or apneic. The manual respirators also performed satisfactorily on the apneic subjects. The manual methods, such as the Schaefer, were inadequate in providing adequate pulmonary ventilation for any length of time in the apneic subject. (However, any sort of manual artificial respiration should be started immediately and continued until a respirator can be obtained.)

2. In administering artificial respiration in the apneic subjects either by respirator or manual methods, the position of the body that provides the minimal resistance to pulmonary ventilation was found to be: (1) hyperextension of the head on the cervical vertebrae, (2) support of the lower jaw from below and (3) the body flat or in a slight Trendelenburg position without pillows under the head. An airway tube may be used; however, in the present studies with respirators the use of such a tube did not result in a significant change in ventilation rate. An endotracheal tube with an inflatable rubber cuff on the end definitely decreases the resistance to artificial respiration in the apneic subject, and this was the most satisfactory arrangement for using type 1 on apneic subjects for long periods of time. The regulator line pressure may be set much lower (10 to 15 cm. of water) with the endotracheal tube and still maintain proper cycling of the respirator and adequate pulmonary ventilation. The falling back of the tongue with blockage of the airway has not been a problem in preventing adequate ventilation with the respirators. Excess fluids and secretions if present should be removed by suction. The proper position of the head should be secured as quickly as possible, for in administering artificial respiration with respirators this is a most critical factor in determining success or failure.

3. The apneic subject in need of artificial respiration should be given 100 per cent oxygen, preferably with the automatic respirators. Studies on the arterial blood before treatment revealed low oxygen saturation, increased carbon dioxide content and a decreased p_H. The addition of 5 per cent carbon dioxide with oxygen would only increase the acidosis.

4. No signs or symptoms of acapnia or tetany were observed even in those subjects with decided hyperventilation (over 15 liters per minute) during artificial respiration. The average changes in p_H and pCO_2 with the automatic respirators producing ventilation rates from 5 to 15 liters per minute were not enough to produce clinical signs of alkalosis.

5. The decrease in cardiac output was variable, large decreases (30 to 40 per cent) occurring in some instances and no decrease in others on line pressures necessary for adequate ventilation. This observation has been correlated with the type of the mask pressure curve present rather than with a particular respirator.

6. The automatic and manual respirators, if properly adjusted, did not produce undesirable effects on the circulation when line pressures adequate to give pulmonary ventilation in apneic subjects were used. All the respirators studied were satisfactory for use and far superior to the manual methods of resuscitation.

7. The ideal mask pressure curve should increase gradually during inspiration to a peak not higher than about 25 cm. of water. The pressure should drop rapidly after reversal, in the beginning of expiration, decreasing quickly to or near atmospheric, with a mean mask pressure during the expiratory period as near as possible to atmospheric. Inspiratory time should not exceed expiratory time.

8. The type of mask pressure curve described in the preceding paragraph permits the right side of the heart to compensate during expiration. From a detailed study of the variations in net filling pressure in the right side of the heart, evidence has been presented indicating that the stroke volume decreases during inspiration due to increased pressure in the thorax. The time and pressure during expiration should be adjusted in such a manner that the total inspiratory cardiac output deficit can be made up by a sufficient

number of heart beats in expiration having a normal or increased stroke volume.

9. Although all the respirators performed in a satisfactory manner in producing adequate artificial respiration, the following criticism may be given for the design of each type as far as concerns the shape of the mask pressure curve produced by it.

Type 1, a pressure-sensitive respirator, may be improved to give a more nearly ideal physiologic performance by a modification of the valves so that the mask pressure curve at the beginning of expiration decreases quickly to or near atmospheric, with a mean mask pressure during the expiratory phase as low as possible. The performance of this apparatus was remarkable over long periods of time; it is easy to clean and sterilize. The plastic model was unsatisfactory due to the warping of valves and the danger of breaking the outside wall.

Type 3, a flow-sensitive respirator, produced an unfavorable type of mask pressure curve because (1) the expiratory time interval is to short and (2) the minimal pressure at the end of expiration is plus 2.5 cm. of water. This instrument was designed primarily for aviation use, and the increased expiratory pressure was advantageous at high altitude; however, the short expiratory period is undesirable even at high altitude with respect to the ideal mask pressure curve based on physiologic studies in man.

Type 4, another flow-sensitive respirator with the various adjustments provided, was an ideal research instrument for studying the numerous variables involved in intermittent pressure breathing and various types of mask pressure curves in relation to changes in cardiac output. The design is complex and the operation requires constant supervision by trained personnel. However, employing the basic principle of design, flow primarily, in contrast to pressure as on type 1, satisfactory production model respirators may be made. The expiratory flow outlet on commercial models of type 4 should be separate from the main respirator mechanism so that vomitus or secretion cannot be blown in the device and jam the reversing mechanism.

Type 5, an example of the "suck and blow" type, was slightly less capable of overcoming breathing resistance in the apneic subject as compared to the intermittent positive pressure models. The negative pressure phase has not been found advantageous over simple intermittent positive pressure. However, no harmful effects were observed when the "suck and blow" was used for one hour in 2 cases of deep coma. There was no evidence in this study that the negative pressure phase aided the circulation. The mechanical performance of the device was satisfactory.

Type 2 produced a mask pressure curve similar to that of type 1, which has already been discussed. The mechanical performance of this model was satisfactory.

Type 6, a manually operated respirator, produced a fairly satisfactory mask pressure curve. The expiratory valve should open more quickly and allow the pressure to drop more rapidly to atmospheric. The sliding valve arrangement was considered unsatisfactory, because the inexperienced operator may block effective ventilation by getting his hand in the way of the sliding part.

Type 7, another manually operated respirator, gave a very desirable type of mask pressure curve. The operation of this model was smoother and safer than that of type 6.

10. In the types of intermittent positive pressure respiration produced by mouth to mouth insufflation, by applying pressure on an anesthesia rebreathing bag or by manual respirators the operator controls the time ratio of inspiration to expiration. It is extremely easy to allow a slightly longer expiratory than inspiratory time period, which permits more heart beats during expiration and allows the heart to make up for the decreased output occurring during the phase of increased pressure in the thorax.

11. Oxygen, helium and oxygen mixtures, and compressed air are too dry for prolonged use on conscious subjects (such as those who have poliomyelitis with complete respiratory paralysis) with intermittent positive pressure respirators. Some form of humidification is necessary for the dry tank compressed gases.

12. Intermittent positive pressure can be used as a means for administering artificial respiration without decreasing cardiac output when the pressure and time for inspiration and expiration are properly regulated.

SANBORN VISO-CARDIETTE ACCEPTABLE

Manufacturer: Sanborn Company, 39 Osborn Street, Cambridge 39, Mass.

The Sanborn Viso-Cardiette is a direct-writing electrocardiograph. The records appear in permanent form on plastic-coated paper. The machine requires a 110 volt, 60 cycle alternating current and consumes 70 watts. The galvanometer is connected with a stylus bearing a heated point which records data on temperature-sensitive paper. A control is provided to adjust the temperature of the point. The recordings obtained in this way are not easily marred, nor are they affected by direct sunlight. Reloading of paper is easy.

The specimen submitted to the Council office for examination was sent to a special investigator for physical tests, as well as clinical trial, in the light of the Minimum Requirements for Acceptable Electrocardiographs as published in THE JOURNAL, 134: 455 (May 31) 1947

1. *Recording Mechanism.* - The investigator reported that the foregoing statements concerning the recording mechanism were accurate.

2. *Sensitivity and Adjustability.* - External voltage sources, both alternating and direct, were connected with various leads through a series resistance of 2,000 ohms, as directed in the requirements. It was shown that the response of the instrument to its incorporated standardizing signal of 1 millivolt was within a range plus or minus 5 per cent of the response to the externally applied signal, and that the test signal voltage could be maintained for a period of two or more seconds. It was noted that the maximum sensitivity was 700 microvolts per centimeter. There was a slight wandering of the stylus from its adjusted base line during normal operation due to alternating current line-voltage fluctuations.

3. *Amplitude Response at Various Frequencies.* Amplitude response recordings of direct versus alternating current signals were obtained at frequencies of 1, 2, 5, 10, 15 and 40 cycles per second, and an external signal generator was swept through frequencies from 40 to 300 cycles per second, while the stylus deflection was measured in millimeters.

4. *Decay Characteristics.* - The response of the instrument at 0.2 second after the application of a direct current of 1 millivolt was compared with the response at 0.04 second.

5. *Relation of Deflection to Voltage.* - The magnitude of the stylus deflection was measured for every step of 100 microvolts from plus 2,000 through zero to minus 2,000.

6. *Adequacy of Grounding.* - With the electrocardiograph connected as for previous tests, and with a millivolt of external direct current pulse applied to the input terminals, the sensitivity was adjusted to give a 1 cm. deflection, and a recording was obtained. The input terminals were then shorted together, and the same signal was applied between this point and the ground of the instrument. There was no response under this latter condition. Increasing the input signal to 100 millivolt gave a 0.5 mm. deflection.

7. *Timing Mechanism.* - A synchronous motor actuates a contractor and provides one second time signals; these can be recorded with any of the leads.

8. *Shock Hazard.* - Although the instrument did not carry an "Underwriters' Listed" label, there was no measurable voltage at the patient cable leads and ground at any setting of the leads-selector switch.

The firm complied with all requirements as regards advertising material and promotional methods. The Council on Physical Medicine voted to include the Sanborn Viso-Cardiette in its list of accepted devices.

DAZOR SUN-HEAT LAMP FIXTURE ACCEPTABLE

Manufacturer: Dazor Manufacturing Corp., 4481-4487 Duncan Avenue, St. Louis.

The Dazor Sun-Heat Lamp Fixture is of the pedestal-type having a circular cast iron base. Above the base there rises an upright bearing the switch box and the pivot for the floating arm bracket. The bracket consists of two arms hinged together so that the maximum reach is 61 cm. (24 inches). At the far end of the outer arm there is a reflector housing that contains a plastic heat-resistant handle for positioning. The fixture as a whole is sturdy and attractive in appearance and bears the approval of the Underwriters' Laboratories.

Bulbs are not furnished with the fixture. It is, however, especially useful in connection with R S sun bulbs drawing 275 watts on 110 to 125 volts alternating current supplies and R-40 heat bulbs drawing 250 watts on 110 to 125 volts alternating or direct current supplies. The diameter of the base is about 30 cm. (12 inches), and the whole weighs 11.3 Kg. (24 7/8 pounds); the shipping weight is 17 Kg. (37½ pounds).

The apparatus was studied by an investigator for the Council, and was found satisfactory. The Council on Physical Medicine voted to include the Dazor Sun-Heat Lamp Fixture in its list of accepted devices.

WHIRLPOOL CARRIAGE, MODEL A, ACCEPTABLE

Manufacturer: Whirlpool Carriage, Inc., 113 East State Street, Westport, Conn.

The Whirlpool Carriage is a portable device for agitating the water in a bathtub or basin. It can be trundled alongside the tub; the casters can be either released or locked. The top of the apparatus can then be raised, rotated through an angle of 180 degrees, and lowered into the water. The stirring mechanism, as it is rotated into place over the water, will clear the brim of the tub at a height of 51 cm. (20 inches) above the floor; by tilting the base, it can be made to clear a brim of 61 cm. (24 inches) above floor level. The usual precautions must be observed to guard against shocks from the use of electric equipment near water; a ground wire is to be clipped to a good ground contact.

The motor connected to the agitator requires a 110 to 115 volt alternating current and draws 650 watts. The base of the apparatus is finished in a white-cream enamel. The total weight of the apparatus is 40.8 Kg. (90 pounds); the shipping weight is 97 Kg. (216 pounds). Its height when not in use is 64 cm. (25 inches).

When examined by an investigator for the Council, the apparatus was found to be of sturdy construction and neat appearance. Additional evidence from other sources acceptable to the Council corroborated the investigator's report of satisfactory performance. The Council on Physical Medicine voted to include the Whirlpool Carriage, Model A, in its list of accepted devices.

ALOE "HELIOGRID" COLD RAY QUARTZ LAMP ACCEPTABLE

Manufacturer: A. S. Aloe Company, Olive at Nineteenth Street, St. Louis.

The Aloe "Heliogrid" Cold Ray Quartz Lamp is a source of ultraviolet light using mercury vapor in a "body grid" composed of "84 inches (238.76 cm.) of pure fused quartz with special graded leakproof seals." This grid is mounted in a spun steel head finished in bronze and trimmed with chromium. The over-all height is 170 cm. (67 inches). The lamp is adjustable vertically and horizontally. The base, equipped with 2 inch (5.08 cm.) casters, houses the transformers. The lamp operates on 115 volts alternating current and draws 40 watts. It is equipped with a built-in timer adjustable for periods from a few seconds to five minutes.

The lamp submitted by the firm was sent to an investigator. He reported that an exposure of 60 to 75 seconds with the grid applicator at 60 cm. produced a perceptible erythema in twelve hours. The lamp is well constructed and of good appearance. The grid applicator was easily adjustable; the orificial applicator was well made and easy to manage. A rayon sleeve is provided to be used over the orificial applicator tube. The exposure guide accompanying the apparatus seemed accurate enough for general use by a physician.

Since this lamp met the erythema dose requirements established by the Council on Physical Medicine of the American Medical Association for cold quartz lamps and in view of the good construction of the lamp, the Council voted to include the Aloe "Heliogrid" Cold Ray Quartz Lamp in its list of accepted devices.

DUREX DIAPHRAGMS, INTRODUCERS AND FITTING RINGS ACCEPTABLE

Manufacturer: Durex Products, Inc., 684 Broadway, New York.

Durex Products, Inc., submitted the following devices to the Council on Physical Medicine: Deep Dome Dumas Diaphragms, Shallow Dome Diaphragms, Duraflex Diaphragms (Matrisalus), Coiled Spring Diaphragms, Mensinga Diaphragms (Flat Spring), Bow-Bend Diaphragms, Coiled Spring Measuring Rings, Individual Diaphragm Introducers and Mayer Diaphragm Introducers.

These devices were referred to an investigator specializing in gynecology for examination and report. Their construction and the evidence for their effectiveness and safety were declared satisfactory. The investigator also reported that the products satisfied the Requirements for Acceptability of Contraceptive Devices recorded in THE JOURNAL (132: 991 [Dec. 21] 1946).

The Council on Physical Medicine voted to include the Durex Diaphragms, Introducers and Fitting Rings in its list of accepted devices.

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SATURDAY, MAY 22, 1948

EDITORIAL ANNOUNCEMENT

The absence of the compositors from their work continues. This issue of THE JOURNAL has been prepared in part by the use of Vari-Typer machines.

RICKETTSIALPOX, A NEW RICKETTSIAL DISEASE

Reports of cases of an acute febrile disease of unusual character were first received by the New York City Department of Health toward the end of June 1946. Sussman[1] reported a recent increase of cases of a peculiar "spotted fever" disease which appeared in the housing development in Kew Gardens, Queens. The clinical appearance resembled that of typhus. The failure to cause agglutination with the usual antigens distinguished the condition from known diseases. Shankman[2] examined more than 60 patients presenting similar symptoms during the same period in the three block square area of Regency Park. The area involved was infested with mice and rats so that the possibility of a rickettsia or virus etiology was strongly suggested.

A joint study by the New York City Health Department and the United States Public Health Service of 144 nonfatal cases of this disease[3] helped to establish the disease as a definite clinical entity for which, because of some similarity to chickenpox, the name rickettsialpox was suggested. The disease is characterized by the appearance of an initial lesion about a week before the onset of fever, chills, sweats, headache and backache and by the appearance of a maculopapular and papulovesicular rash about three to four days after the onset of fever. Except for leukopenia, routine laboratory results are generally negative. The usual bacterial agglutination tests are uniformly negative; however, antibodies for rickettsialpox are demonstrable by means of the complement fixation test. There have been no deaths. Blood cultures were negative in all of the patients. Agglutination tests for typhoid bacilli, paratyphoid bacilli A and B, Brucella, Leptospira icterohaemorrhagiae, Leptospira canicola and Pasteurella tularensis were done with the serums of 30 samples of blood obtained from patients in both the acute and the convalescent stages. Agglutination tests for Proteus OX19 and OX2 were done with the serums of a considerable number of recovered patients. With the exception of a few that agglutinated in low titers, all were negative.

Huebner[4] and his associates at the National Institute of Health isolated from each of 2 patients with this disease an organism proved to be a rickettsia. This organism produced illness in mice and guinea pigs and grew well in the yolk sacs of fertile eggs. Ether-extracted yolk sac antigens were prepared which fixed complement with convalescent serums drawn from typical cases. "Cross tests" with immune serum and antigens from other species of rickettsia demonstrated that this strain is antigenically distinct from the organisms causing typhus, tsutsugamushi and Q fever. The reaction appeared to be specific except for the cross reactions with Rocky Mountain spotted fever. The behavior of the isolated organism resembled that of Rickettsia conori, the causative agent of fièvre boutonneuse, except for the failure of the disease under study to stimulate agglutinins for strains of Proteus OX 19 and OX 2 in the serums of most of the New York patients.

The basements of the dwellings in which some of the cases occurred were infested with mice and with the rodent mite Allodermanyssus sanguineus. Huebner[5] and his associates recovered a rickettsia from a saline suspension of the tissues of mites and a rickettsia which was morphologically, culturally and serologically similar from a mouse "bitten" by A. sanguineus. The behavior of the two mite strains in producing disease in guinea pigs, mice and chick embryos and as antigens in the complement fixation tests seem to establish them

1. Sussman, L.N.: New Gardens' Spotted Fever, New York Med. 2:27 (Aug. 5) 1946.

2. Shankman, B.: Report on an Outbreak of Endemic Febrile Illness, Not Yet Identified, Occurring in New York City, New York State J. Med. 46:2156 (Oct. 1) 1946.

3. Greenberg, M.; Pellitteri, O.; Klein, I.F., and Huebner, R.J.: Rickettsialpox, J.A.M.A. 133:901 (March 29) 1947.

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as identical with the strain of rickettsialpox isolated from the patients. Further evidence of this identity has been provided by solid immunity afforded guinea pigs by rickettsialpox against one of the mite strains. Apparently identical strains of rickettsia from a man ill with rickettsialpox and from bloodsucking mites collected from the domicile of the same man indicate that human infection is acquired from the mites probably through biting. The authors suggest the name Rickettsia akari for this newly discovered microorganism of the rickettsial group.

MENTAL HOSPITALS: NEW YORK

The Committee on Public Health Relations of the New York Academy of Medicine[1] has recently reported on problems of the New York state mental hospitals system. Administrators of such hospitals face numerous problems, but they are especially concerned with provision of care for more patients than the rated capacities of their institutions. Public indifference to the fate of mental patients is still reflected by the depersonalization of care rendered in mental hospitals. Research programs connected with the mental hospital system are badly needed. The principal problems are overcrowding, understaffing, insufficient funds and deteriorated physical plants. Immediate recommendations call for correction of existing overcrowding by systematic review of patients, with discharge of patients in convalescent state or to family care. Expansion of the program of family care is desirable to secure increase in numbers of foster homes for mental patients and establishment of proper levels of payment. An effort should be made to attract competent personnel by providing adequate salaries and good living conditions. Proper investigation is necessary to obtain larger payments from relatives of patients. Repair of existing deficiencies in physical plants is necessary with advice from expert architects. Present inadequacy should be brought to the attention of the public and legislative bodies. The committee recommends long term planning to formulate a definite, integrated policy for future care. Institutional units should be limited to not more than 3,000 beds. New mental hospitals need to be located near large urban centers, so that they may affiliate with teaching institutions. Experimental hospital units for new approaches to treatment are necessary. An attempt should be made to establish sufficient numbers of psychiatric clinics to insure proper preventive outpatient care and treatment. The staffs of mental hospitals should be qualified to conduct research in the physiologic as well as psychologic factors of mental disease. Psychiatric service must provide comprehensive training programs for both young psychiatricts and general interns and special provision should be made for graduate training of psychiatric nurses, social workers, clinical psychologists and other needed auxiliary personnel. Finally, the public should be thoroughly enlightened concerning mental illness, its prevention and the needed facilities for treatment.

The committee report on conditions and needs in the mental health field of New York state mirrors completely conditions and needs in mental health throughout the United States.[2] Mental health is outstandingly a leading medical, public health and social problem.

Throughout the nation funds are insufficient for improvement of physical plants, increased facilities for training of personnel and increased research. Present knowledge offers the greatest hope for improvement of mental health in the United States by a concerted attack in the preventive field. Goals have been set which demand availability of at least one mental hygiene clinic per hundred thousand population. While this goal has by no means been reached today, the immensity of the problem would in all likelihood still make it insufficient. The need is certain to be increased once a properly educated public is relieved of its tendency to avoid obtaining psychiatric aid even when they themselves recognize the need.

No other field of health is as greatly handicapped by social stigma as is mental ill health. This handicap will be diminished and real needs supplied only by a greatly intensified program of public education wherein responsibilities are made known and the implications of personal and collective social attitudes in determining mental ill health are made clear

Current Comment

REGISTRATION UNDER THE HARRISON NARCOTIC ACT

Physicians who are registered under the Harrison Narcotic Act or under the Marihuana Tax Act must effect registration on or before July 1 to avoid a penalty. Each year, despite the annual warnings in THE JOURNAL, this requirement is overlooked by some physicians and unpleasant consequences follow. Failure to register adds a penalty of 25 per cent to the tax payable and in addition subjects the physician to the possibility of a fine not exceeding $2,000 or to imprisonment for not exceeding five years, or to both. As an act of grace the Commissioner of Internal Revenue has in past years given some tardy registrants the choice between paying sums by way of compromise, a procedure authorized by law, or accepting criminal prosecution. If this procedure does not produce the required promptness in reregistration, the commissioner will have no other alternative than to institute criminal prosecution.

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2. Situation in Psychiatry, Miscellany, J.A.M.A. 137:212 (May 8) 1948. Menninger, W. C.: Facts and Statistics of Significance for Psychiatry, Bull. Menninger Clin. 12:1-25 (Jan.) 1948.

WHICH KENNETH WALKER WILL YOU HEAR?

About a year ago THE JOURNAL received a complaint from England that misrepresentations were occurring with respect to the identity of an American lecturer named Kenneth Walker. A distinguished Fellow of the Royal College of Surgeons has the same name. Contact was made with the American lecturer; he wrote that only recently had he become aware of the identity of the English surgeon and he asserted that the misrepresentation in promotional material being used by a booking agency in his behalf had come about rather innocently. The American lecturer had left a copy of a book written by the English physician in an office where an unnamed employee had accidentally seen it and assumed at once that the American was the author. Distribution of the erroneous piece of promotional literature, according to the American Kenneth Walker, had been stopped. Now Dr. Kenneth Walker of London, author of the well known book, "Physiology of Sex," has again indicated that there is persistent reliance on the similarity of the names by the American lecturer. The American Kenneth Walker has appeared before many gatherings during the past season, using as a subject "Live Together or Live Not." The impression is apparently prevalent that the American, who lectures on personal experiences and observations in foreign countries during the World War just ended, is the eminent English surgeon. A man has exclusive right to his reputation. When his name is the same as that of another man, confusion of repute should be avoided. Abuse of the similarity in names is not only undesirable but unethical and may be damaging. Since the British Kenneth Walker is an eminent physician and the American is not, confusion as to the identity might be especially reprehensible.

AMINO ACID AND VITAMIN INTERRELATIONS

Recent experimental observations on the production of deficiency complexes and their therapeutic control by varying the quantitative and qualitative dietary intake of amino acids and vitamins may have distinct implications as to the etiology and treatment of certain conditions of disease in man. The first observation suggestive of an interrelation between the activity of vitamins and amino acids was provided by Goldberger, who noted that the amino acids tryptophane and cystine exert some beneficial effect in human pellagra, indicating that factors in addition to nicotinic acid may be involved in the production of this disease. Subsequent observations showed that blacktongue, the canine counterpart of pellagra in man, produced by feeding corn grits and a synthetic diet low in nicotinic acid, as well as the growth inhibition in rats under the same diet, can be counteracted by adding tryptophane alone to the diet.[1] Bessey and Wolbach[2] found that in rats on a diet deficient in lysine or tryptophane there developed corneal vascularization similar to that in animals with riboflavin deficiency. Maun, Cahill and Davis[3] reported similar ocular lesions in rats on a diet deficient in leucine. Hueper[4] observed the development of porphyrin incrustations on the snout and ears of rats on a diet low in protein and methionine and deficient in aromatic amino acids (gelatin). These conditions, usually found in certain vitamin deficiencies (riboflavin, pantothenic acid), were not obviated when large amounts of these vitamins were added to the diet. The inhibition of growth exerted on cultures of Streptococcus lactis by excessive amounts of glycine or serine in the medium as well as the toxic effects elicited in animals given abnormal quantities of these amino acids can be prevented by pyridoxine.[5] Daft[6] recently recorded that rats made agranulocytic by feeding a protein-free diet gave granulocytic response when given folic acid; he noted that this action was accentuated when nicotinic acid, methionine and threonine were added. While the granulocytic reaction to the vitamins was rapid, it was slow if the agranulocytic rats were given a mixture of essential amino acids. There appears to be a relationship between amino acid and vitamin deficiencies and the development of blood dyscrasias. The experiments of Wissler and associates[7] revealed that the repletion of protein and the formation of antibodies in protein-depleted adult rats is impaired when these animals are fed a ration adequate in high quality protein but deficient in certain vitamins. It is not likely that the action of the amino acids is due to a direct replacement of vitamins. An adequate supply of suitable amino acids seems to enable the animal organism or its intestinal flora to synthesize vitamins of the proper type. The utilization of vitamins by the organism, on the other hand, seems to be defective unless adequate amounts of amino acids of the proper type are available. Since radical changes in the kind of intestinal bacterial flora and thereby in the quantitative and qualitative production of vitamins by these micro-organisms can be brought about by dietary changes, control of the resultant manifestations of deficiency may be accomplished in certain conditions by varying the quantitative and qualitative intake of proteins. The various observations on the interrelations between the action of amino acids and vitamins may find some practical application in human medicine in connection with the treatment of starvation states, the use of specific amino acid therapy and the causation and control of chemical blood dyscrasias, especially those of the agranulocytic variety.

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4. Hueper, W. C.: Toxicity and Detoxication of Cinchophen; Experimental Studies, Arch. Path. 41:592 (June) 1946.

5. Welch, A. D.: Interference with Biological Processes Through Use of Analogs of Essential Metabolites, Physiol. Rev. 25:687 (Oct.) 1945. Fishman, W. H., and Artom, C.: Serine Injury, J. Biol. Chem. 148:345 (Sept.) 1942.

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V 1
194

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

May 21, 1948

Report Stresses Progress In Medical Care

A report prepared by Dr. George W. Bachman and Dr. Lewis Meriam for the private Brookings Institution, on behalf of the Senator Subcommittee on Health of the Labor Committee, observes that the United States had made great progress in health conditions. It points out that forty years ago the United States was outclassed by leading nations, while today the health of the white population is better than that of larger western European nations. It is on a par with the small nations with the best records. Health of Negroes is less favorable because of economic and social reasons, rather than lack of medical care. The report also states that there are not enough physicians to meet demands of a compulsory health insurance system.

Further Delay In Clearing World Health Bill

Although the House Republican Steering Committee had cleared legislation to permit the United States to join the World Health Organization, further delay was encountered in getting this bill out of the Rules Committee. The Republican Committee checked major legislation in advance of the scheduled June 19 adjournment and included the measure among bills slated for action this week. The Senate passed the W.H.O. bill unanimously last year and the House Foreign Affairs Committee approved it unanimously, but the Rules Committee blocked action on it. This barred the United States from charter membership in the World Health Organization and presented a strong propaganda weapon to forces opposing the democratic system of government. The State Department is in favor of congressional action so that the United States can take part in the meeting of the World Health Organization in Geneva, Switzerland, in June.

Delegates Make Capital A Medical United Nations

The two thousand delegates from all over the world to the fourth International Congresses on Tropical Medicine and Malaria gave the national capital the semblance of a medical United Nations. Sessions were conducted in English, French and Spanish, and local hotels had delegates registered from around the globe. The federal government sponsored the conference through the State Department and six other agencies, with the cooperation of fifteen national professional societies and several intergovernmental agencies. A total of one hundred and fifty societies and sixty governments received invitations, and one hundred and eighty papers from outstanding scientists of thirty seven nations were read. The scientific program was conducted in twelve sections, with as many as four meetings being held simultaneously.

U. S. Public Health Service Appointments

Surgeon General Leonard A. Scheele of the U.S. Public Health Service announced the appointment of the new deputy chief, Dr. W. Palmer Dearing of Chevy Chase, Md., and other division heads. Dr. Dearing is deputy Surgeon General and as second in command will serve as Surgeon General in Dr. Scheele's absence. He succeeds Dr. James A. Crabtree, who will direct medical mobilization planning for the National Security Resources Board. Dr. Bruce D. Forsyth was named assistant surgeon general and chief of the Dental Division, succeeding Dr. William Wright Jr., who has been transferred to duty with the Bureau of Employes Compensation, Federal Security Agency, and the Bureau of Indian Affairs, Department of Interior. Dr. Eugene A. Gillis succeeds Dr. Dearing as head of the service's Division of Commissioned Officers. He has been assistant chief. The appointments became effective May 17.

National Nutritional Yardstick Lowered By Council

The National Research Council reported at its conference here that the national nutrition yardstick has been reduced by the food and nutrition board. The daily calory allowances for sedentary persons has been dropped 100 calories below previous recommendations, with the claim that the original figure had been shown by studies since 1941 to be higher than persons actually need. The previous limit was said to be likely to cause too great an increase in weight for good health.

Amputees Win Awards For Testing Artificial Limbs

Robert S. Allen, newsman who served overseas as press chief for the late General George S. Patton Jr., was one of fifteen amputees who have been honored by the Army for "outstanding and patriotic service in testing artificial limbs and furthering the general program of research and development in the field of prosthetics." Secretary of the Army Kenneth C. Royall presented the certificates to three recipients in Washington, D. C., and army commanders in other areas were to make similar presentations to twelve others. Mr. Allen is consultant to the Committee on Artificial Limbs and cooperates with the Army Prosthetic Research Laboratory, the Mare Island Naval Hospital limb shop and Northrop Aircraft, Inc., in the development of artificial limbs and devices.

Medical Legislation

Michigan

Bill Enacted.—H. 14-XXX has become public act 14 of the Acts of 1948. It amends the hospital survey and construction act by providing that any hospital receiving federal aid under the federal hospital survey and construction act shall comply with the minimum standards of maintenance and operation which the state department of public health with the advice of the advisory hospital council shall promulgate.

Rhode Island

Bills Enacted.—H. 604 was approved April 30, 1948. It requires the enrichment of bread and flour by the addition of certain vitamins and minerals for the better protection of the public health. H. 658 was approved April 30. It provides for an act to extend and strengthen the mental health services in the state and designates the state department of social welfare as the agency to cooperate with the federal government in this regard. H. 743 was approved April 30, 1948. It provides for the licensing, regulation, inspecting and examination of homes for the aged or convalescent persons.

South Carolina

Bill Enacted.—H. 1214 has become Governor's Act 1156 of the Acts of 1948. It puts sulfanilamide, sulfapyridine, sulfadiazine, aminopyrine, thyroid and other antifat preparations, together with any other drugs declared to be "dangerous drugs," on a prescription basis.

GOVERNMENT SERVICES

ARMY

MEETING OF CONSULTANTS

The Advisory Council of the Society of United States Medical Consultants in World War II met in the Surgeon General's Office May 8 to discuss future planning related to medical department personnel, revision of tables of organization, a new system of unit mobilization, problems of training and education and plans for medical reserve officers. Among those present were: Drs. Frank B. Berry, president; Henry M. Thomas Jr.; M. Ralph Kaufman; Alfred R. Shands Jr.; M. Barnes Woodhall; Donald M. Pillsbury; Yale Kneeland Jr.; Walter Bauer; Perrin H. Long; Ivan C. Berlien; I. Ridgeway Trimble; Francis R. Dieuaide; I. S. Ravdin; Harold A. Sofield; John V. Ambler, and Henry W. Brosin.

NEW VENEREAL DISEASE CONTROL FILM

More than one thousand four hundred educators and members of the clergy from the District of Columbia, Maryland and Virginia were invited to see March 10 the Army's new training film on veneral disease control, "Miracle of Living." The film, which is the only one currently in use for this purpose, emphasizes the moral approach to anti-venereal disease hygiene. The group was addressed by Kenneth C. Royall, Secretary of the Army, Major Gen. Raymond W. Bliss, the surgeon general, and Major Gen. Luther D. Miller, chief of chaplins. Lieut. General Willard S. Paul, director of personnel and administration, department of the Army, and president of the Army Venereal Disease Control Council, presided. A discussion was conducted after exhibition of the film, thus typifying the Army's policy of seeking civilian counsel and participation in the formulation of policies in moral and educational matters.

AWARDS AND COMMENDATIONS

Captain Harold F. Rheinlander

Capt. Harold F. Rheinlander, M.C., A.U.S., of Washburn, Maine, has been awarded the Army Commendation Ribbon for meritorious service for the period April 1946 to March 1948 as assistant chief of surgical service and then chief of surgical service, Regional and Station Hospital, Maxwell Air Force Base, Montgomery, Ala. Dr. Rheinlander graduated from Harvard Medical School, Boston, in 1944 and entered military service in April 1946.

Captain John C. Jarrett

Capt. John C. Jarrett, M.C., A.U.S., of Ellwood City, Pa., has been awarded the Army Commendation Ribbon for meritorious service for the period April 1946 to March 1948 as chief of obstetrical and gynecology service, Regional and Station Hospital, Maxwell Air Force Base, Montgomery, Ala. Dr. Jarrett graduated from Western Reserve University School of Medicine, Cleveland, in 1945 and entered military service in April 1946.

Captain Edmund D. Pellegrino

Capt. Edmund D. Pellegrino, M.C., A.U.S., of Brooklyn, has been awarded the Army Commendation Ribbon for meritorious service for the period April 1946 to March 1948 as assistant chief and then chief of medical service, Regional and Station Hospital, Maxwell Air Force Base, Montgomery, Ala. Dr. Pellegrino graduated from the New York University College of Medicine, New York, in 1944 and entered military service in April 1946.

AIR FORCE

AVIATION PHYSIOLOGISTS

Seventeen medical corps officers graduated April 16 from the aviation physiologists' course at the School of Aviation Medicine, Randolph Field, Texas. Among the graduates were Lieut. Col. Francisco Sureda and Second Lieut. Amilcar Augusto, Air Force of Uruguay, Capt. George Cantoni, Air Force of France, and Lieut. Hilmi Dinc, Air Force of Turkey. The course is offered to medical officers who complete the aviation medical examiners' course. It prepares graduates to indoctrinate flying personnel on the changes in body functions at high speed and altitude. Counteraction, prevention and treatment of these physiologic changes form a major part of the instruction given to students. Col. Don Flickenger, Medical Corps, director of medical sciences, addressed the graduating class.

PROMOTIONS

John M. Hargreaves, deputy air surgeon, has received a temporary promotion to brigadier general in the medical corps of the Army. General Hargreaves, a native of Illinois and a graduate of the University of Minnesota Medical School, entered the service in 1925 and after graduating with honors from the School of Aviation Medicine in the following year was attached to the Air Forces, in which he has served since. He is also an honor graduate of the Army Medical School, a graduate of the Medical Field Service School and the Command and General Staff School. General Hargreaves was chief surgeon of the 8th Air Force on Okinawa during the recent war and later surgeon of the Pacific Air Command with headquarters at Manila and later at Tokyo.

Col. Harry G. Armstrong, commandant, Air University School of Aviation Medicine, Randolph Field, Texas, has been promoted to the rank of brigadier general. General Armstrong graduated at the University of Louisville School of Medicine and entered the Army in 1929. During World War II he was surgeon of the 8th Air Force in the European theater of operations and also surgeon, Armed Forces Division, Office of Military Government (United States) Berlin, Germany. His "Principles and Practice of Aviation Medicine" is a standard textbook throughout the world. In recognition of his work he has received the Collier Trophy and the John Jeffries award and has been decorated by England, France, Belgium and Poland.

BORDER HEALTH ASSOCIATION

Recently the United States Mexico-Border Health Association held a conference at Laredo, Texas, and Nueva Laredo, Mexico. Lieut. Col. Kenneth E.

Pletcher, M.C., from the School of Aviation Medicine, Randolph Field, Texas, was among the speakers. Following the conference, Dr. David Glusker, México, D.F., and Lieut. Col. Patricio Y. Funtes, commandant of the Indoctrination Center, Army of Mexico, visited Randolph Field and the Preventive Medicine Department and its allied research unit at the School of Aviation Medicine.

SCHOOL OF AVIATION MEDICINE

Dr. Gunnar Lundin of Sweden and Dr. Vogt Lorentzen of Norway, Scandinavian aviation physiologists, visited the School of Aviation Medicine, Randolph Field, Texas, to study laboratory procedures in aviation medicine. Sweden is in process of establishing a School of Aviation Medicine on the basis of the requirements at the Air University School of Aviation Medicine at Randolph Field.

AWARDS AND COMMENDATIONS

Major Cortez F. Enloe Jr.

Major Cortez F. Enloe Jr., now of Manhasset, Long Island, N. Y., has been awarded the Air Medal. The citation reads as follows: For meritorious achievement while participating in aerial flight in the China-Burma-India Theatre from February 1944 to May 1944. As Flight Surgeon with the First Air Commando Force, Major Enloe contributed to the success of combat operations and the aerial evacuation of wounded from behind enemy lines. The exceptional courage, professional skill and devotion to duty exhibited by Major Enloe while engaged in missions of unusual hazard reflected great credit on himself and the Army Air Force.

Dr. Enloe graduated from Friedrich Wilhelms Universität Medizinische Fakultät, Berlin, Germany, in 1937 and entered the military service of the United States in September 1942.

NAVY

RESEARCH ON TROPICAL DISEASES

The Naval Medical Research Unit, which is a part of the University of California's African Expedition, arrived in Africa in February to begin a year's study of tropical diseases. It traveled through the agricultural areas of Egypt, the Libyan Desert and the Assuan Mountains. A Bedouin guide led the party through the unbroken terrain of the desert and mountains. On reaching Wadi Halfa the Company ferried the equipment to the east bank of the Nile and opened the first temporary research laboratory in a government rest house. The Nubian Desert from Wadi Halfa to Abu Hamed was worked for zoologic as well as medical specimens. Fox, jackal, hyena, gazelle, reptiles and small game abound in this area; the only birds noted were white vultures and black ravens. In considering human diseases found in the Nubian area, Commander J. M. Amberson, MC, Commandant, reports they are similar to those normally occurring in persons of the temperate zones. Malaria, bilharzia, and trachoma are prevalent. Rheumatism, arthritis and diabetes are frequently found among the Nubians. Tropical diseases are found in the Northern Sudan. At Wadi Halfa and Abu Hamed portable x-ray machines were set up, giving the natives their first experience with x-ray. Through this project numerous diagnoses were made of fractures, renal stones, arthritic changes, pleural effusions, tuberculosis, enlarged hearts and osteomyelitis. The inhabitants of the Nubian area were examined by the medical officers to get a cross section of the diseases found there. Asthma is prevalent and found to be caused by hordes of chironomid flies. Another pest, the black fly (Simulium damnosum) attacked the group every afternoon, and its bite caused profuse bleeding. Though not a disease transmitter at Abu Hamed, this fly is infected at Dongola and in the southern Sudan, and in some areas it causes epidemic blindness.

The Naval Medical Reserve Unit now in the Anglo-Egyptian Sudan has trapped eight living shrews, some of them infected with malaria. The shrew, a mouselike creature, rare in captivity, was reported in 1913 to be infected with an undefined type of malaria, and the present report confirms this. These shrews will be sent to Washington, D. C., and placed in the care of the director of the National Zoological Park and of Dr. Clay Huff of the parasitology Department, Naval Medical Research Institute, Bethesda, Md. The Navy considers that the capture of these animals may prove of great importance in the evaluation of new chemical drugs having possible curative action on malaria.

NEW REGULAR OFFICERS

The following lieutenants (junior grade) have transferred from the Medical Corps Reserve to the Regular Navy Medical Corps: William L. Chapman, Warren, Pa.; Charles R. Sullivan, St. Petersburg, Fla., and Gilbert A. Webb, Oakland, Calif. All are graduates of the Navy's V-12 program.

The following physicians from civil life have accepted temporary appointments in the Regular Navy Medical Corps: Lieut. (jg) John J. Flahive, Springfield, Mass., and Lieut. (jg) Roy S. Ogren, Palo Alto, Calif.

Lieut. Carl E. Pruett of Kinmundy, Ill., U.S.N.R., has been nominated for active duty pending his acceptance of appointment in the Medical Corps of the Regular Navy.

Comdr. John J. Brown of Bellerose, N.Y., U.S.N.R., has accepted appointment in the regular Navy Medical corps.

Lieuts. (jg) William R. Thomas of Akron, Ohio, and Robert R. Sexton of Ipave, Ill., both graduates of the Navy's V-12 program, have accepted appointments in the regular Navy Medical Corps.

OFFICERS APPROVED FOR GRADUATE TRAINING

At a meeting in April of the Advisory Board to the Bureau of Medicine and Surgery, the following Navy Medical Officers were approved for graduate training:

Comdrs. E. E. Hogan of Oxford, N. Y., and R. R. Rambo of South Bend, Ind., to continue law course at the George Washington University School of Law.
Comdr. Harold A. Streit of Algona, Iowa, fellowship in orthopedic surgery at the Cleveland Clinic.
Comdr. John S. Thiemeyer Jr. of Norfolk, Va., extension of present course in Children's Orthopedics at the Children's Hospital, Boston.
Comdr. Joseph L. Yon of Charlottsville, Va., residency in surgery, Naval Hospital, Great Lakes, Ill.
Lieut. Howard W. Hill of Oakland, Calif., residency in surgery, Naval Hospital, Oakland.
Lieut. Jack S. May of Hyattsville, Md., to continue law course at Catholic University of America, School of Law.

SOCIETY NEWS

Rear Admiral H. Lamont Pugh (MC), assistant chief of the Bureau of Medicine and Surgery, addressed the section on General practice of medicine of the District of Columbia Medical Society, Washington, D.C., on the "The Role of the General Practitioner in Modern Medicine."

VETERANS ADMINISTRATION

HOME TOWN MEDICAL CARE FOR VETERANS

Dr. Paul B. Magnuson, chief medical director, Veterans Administration, writes: "It has come to my attention that considerable misunderstanding has developed throughout the medical profession concerning the establishment of fees for medical services to be paid private physicians participating in the so-called "Home Town Medical Care Program for Veterans." It has been contended that the Veterans Administration has arbitrarily established a fee schedule which represents the maximum amount which may be paid for any given service and which is, in effect, a national fee schedule. It has also been contended that the various state medical societies and other interested groups were not consulted when this fee schedule was adopted.

"In order to clear up any misunderstanding regarding this matter, it is desired to emphasize that my predecessor, Dr. Paul R. Hawley, had no intention at any time of establishing a national schedule of fees, nor do I contemplate doing so. However, the fee schedules originally submitted by the various state medical societies, when the "Home Town Medical Care Program" was inaugurated, varied so widely in format, terminology and fees for similar or identical services that it was deemed advisable to establish a uniform fee schedule format and to set up tentative fees which could be used as a guide by the various state medical societies when submitting their proposals for the furnishing of medical care to veterans.

"This uniform fee schedule format was formulated by the Professional Group of National Consultants to the Chief Medical Director. This group, representing the various specialties in medicine and surgery, is composed of eminent physicians from all parts of the country. Tentative fees were set up in the format after a careful analysis of prepaid medical care plan workmen's compensation and insurance fee schedules, and also the fee schedules in effect in the various states having agreements with the Veterans Administration. As was to be expected, considerable variation occurred in the fee schedules reviewed

"The Professional Group of National Consultants made every effort to arrive at fees that were considered to be within reasonable limits and which would, as nearly as possible, allow a uniform provisional fee schedule for use as a guide in facilitating and expediting the preparation of agreements between state medical societies and the Veterans Administration.

"Further attempt was made to provide for elasticity in the charges for certain operations or other services which seemed to evoke more than average contention by listing the minimum and maximum amounts considered equitable. These items bear the notation "AA," which indicates that the fee for the given service is to be determined by arbitration and agreement between the Veterans Administration and the medical society concerned.

May I reiterate that the Veterans Administration Fee Schedule Format is in no sense to be construed as an arbitrary or national fee schedule. Furthermore, it is subject to periodic review and such modification as conditions may indicate."

VETERAN TRAINING FOR A MEDICAL CAREER

The Veterans Administration announced May 17 that one in every twenty-five World War II veterans training under the G. I. Bill is preparing for a career in medicine or a related field. Of former service men and women, 191,337 were enrolled in educational institutions in training for medical positions ranging from laboratory technicians to surgeons. Of these, 25,293 were enrolled in medical schools and 18,265 were in premedical training; 13,245 veterans were training to become pharmacists and 5,194 to become laboratory technicians and assistants.

Veterans are eligible for educational training benefits if they served in the armed forces between September 16, 1940 and July 25, 1945, had ninety days or more of active service and were released under conditions other than dishonorable.

PUBLIC HEALTH SERVICE

THREE NEW MAJOR GENERALS

The rank of major general has been conferred on three Bureau chiefs of the Public Health Service, according to Oscar R. Ewing, Federal Security Administrator. Elevated in rank from brigadier general were Dr. R. C. Williams, chief, Bureau of Medical Services; Dr. C. L. Williams, chief, Bureau of State Services, and Dr. R. E. Dyer, director, National Institute of Health. The action was under authority of Public Law 425 (S. 1454), passed February 28 by the Eightieth Congress, which amended Public Law 410, Seventy-Eighth Congress, the 'Public Health Service Act."

INCREASE IN RESIDENT PATIENTS

At the end of 1946, 382.4 of every 100,000 persons in the civilian population of continental United States were in hospitals for the prolonged care of psychiatric patients, according to figures of the Mental Hygiene Division of the Public Health Service, released April 21 by the Federal Security Administrator. The number of resident patients increased during the year by 10,595, representing about 2 per cent of the 510,472 present at the beginning of the year. The number of first admissions to prolonged care hospitals during 1946 was 153,025. The figures are based on results of the 1946 Census of Patients in Mental Institutions, collected by the Bureau of the Census. Collection of these data was made a function of the Mental Hygiene Division of the U. S. Public Health Service in February of this year. The statistics, which cover either the calendar year or the fiscal year ending in the calendar year, are for hospitals which provide care for chronic patients although also receiving patients for short periods of time for observation and diagnosis. The statistics on veterans' hospitals are adjusted figures based on tabulations prepared by the Veterans Administration and cover veteran neuropsychiatric patients under the care of the Veterans Administration in federal hospitals of all types. While the figures for state hospitals and for veteran neuropsychiatric patients are substantially complete, reports were not received from an appreciable number of county and private mental hospitals. The over-all coverage, in terms of admissions, is estimated to be between 90 and 95 per cent complete.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

State Medical Election.—At the California Medical Association meeting in San Francisco April 11-14, Dr. R. Stanley Kneeshaw, San Jose, was chosen president-elect and Dr. E. Vincent Askey, Los Angeles, was installed as president.

Establish Section of Allergy.—An Allergy Section of the California Medical Association, to be known as the California Society of Allergy, was organized April 11 by thirty allergists of the state in San Francisco. Dr. Willard S. Small, Pasadena, was elected temporary chairman and Dr. Frank G. Crandall Jr., Los Angeles, temporary secretary. The new section will hold meetings in conjunction with the annual meetings of the California Medical Association. Physicians interested in allergy are invited to attend.

CONNECTICUT

Ferris Lecture.—The eleventh Harry Burr Ferris Memorial Lecture of the Yale Medical Society was given by Melvin H. Knisely, Ph.D., Chicago, May 12, on "Sludged Blood."

Personal.—Dr. John F. Fulton, chairman, Yale University School of Medicine department of physiology, will deliver the William Withering Memorial Lectures at the University of Birmingham, England, June 7-10 on frontal lobotomy. He will also receive the honorary doctor of science degree from the University of Birmingham on July 3. The Withering lectures were established in honor of the graduate of the school who discovered the action of digitalis in 1785.

COLORADO

Lectureship in Surgery.—An annual lectureship in surgery for the University of Colorado Medical School has been established by Dr. Oscar T. Clagett, 1933 alumnus, now chief of the section on thoracic surgery at the Mayo Clinic, Rochester, Minn. The first lecturer will be Dr. Owen H. Wangensteen, professor of surgery at the University of Minnesota.

Postoperative Care of Cancer Patients.—Sands House, Denver, formerly operated for the care of tuberculous women, reopened on March 22 to care for victims of cancer in the Rocky Mountain region. It will accommodate 48 patients in its two wards and twenty private and semiprivate rooms. Operated as a nonprofit association with a staff of twenty members, it is open to men and women patients of all ages on referral by a member of the Colorado State Medical Society. Postoperative care will be provided patients who are unable to secure it in hospitals and private homes.

ILLINOIS

Play Day.—The Champaign County Medical Society is making plans for their "Play Day" on June 10, an afternoon and evening affair to which all physicians in the surrounding counties are invited. There will be golf and other games in the afternoon and a nonscientific dinner in the evening.

Postgraduate Conference.—The Postgraduate Education Committee of the state medical society will hold a postgraduate conference at the Mineral Springs Hotel, Alton, June 3. The session will open with a luncheon sponsored by the Madison County Medical Society. Physicians participating in the program are: Wayne W. Flora, Chicago, anal fissure and fistula; Joseph N. Rappaport, Evanston, behavior problems of early childhood; Philip Thorek, Chicago, preoperative and postoperative therapy; Claude N. Lambert, Chicago, principles of fracture treatment, Walter F. Dillon, Chicago, cancer of the cervix and endometrium; Robert S. Berghoff, Chicago, coronary disease; Thomas D. Mastera, Springfield, management of diabetes during pregnancy; Frederick H. Falls, Chicago, antepartum hemorrhage, and Percy E. Hopkins, Chicago, president, state medical society, Illinois prepayment medical care plan. Dr. Harold M. Camp, Monmouth, secretary of the state society, will speak at the banquet on "Necessity for a Cooperative Program in Providing Medical Care."

Chicago

Dr. Phemister Awarded Honorary Fellowship.—Dr. Dallas B. Phemister, chairman and professor of the department of surgery, University of Chicago, was recently awarded the honorary fellowship of the Royal College of Surgeons of England for outstanding contributions to the pathology of surgical shock and lesions of the bones and joints.

Research on Nucleic Acids.—The American Cancer Society, Inc., has awarded a grant of $18,935 to the department of pathology of the University of Illinois College of Medicine for an investigation of nucleic acids and amino acids in relation to cellular growth. Dr. Isidore Gersh, associate professor of pathology, will serve as the principal investigator.

Cancer Research Hospital.— Construction of the University of Chicago's new cancer research hospital, adjoining the west wing of the University Clinics, was started May 3. The estimated cost will be $2,000,000. The major part of the seven story building will consist of laboratories and facilities for research. Two floors will provide fifty-two beds for patients; another floor will be devoted to outpatients.

KANSAS

Premarital Examinations Lower Marriage Rate.—The Kansas State Board of Health reports that Kansas experienced a 45 per cent drop in the marriage rate for 1947 as compared to 1946, most of which must be attributed to the decrease in marriages following the new marriage laws effective in July 1947. There were only 1,799 marriages recorded in December 1947 as compared with 5,891 for December of the previous year.

MAINE

Cancer Laboratory Fund.—A committee under the chairmanship of J. Anthony Probst, New York, has been organized to raise $1,500,000 for reconstruction and maintenance for five years of the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, that was destroyed last October by forest fires. Dr. Clarence C. Little is chairman of the board of trustees of the laboratory.

MARYLAND

Mental Hygiene Department Established.—A Division of Mental Hygiene has been functioning within the Maryland State Department of Health since January 7. Clinics are being held in seven counties, and plans are under way to establish services in two additional counties. This psychiatric program has been made possible through federal funds allotted to Maryland through the U. S. Public Health Service. The Public Health Service also assigned Dr. Kenneth B. Jones to this state as chief of the

Division of Mental Hygiene. Clinics provide services to all age groups in areas where no other psychiatric diagnosis or treatment is available. Patients are referred by courts, schools, welfare organizations, social service agencies, children's agencies, health officers and private physicians. Persons who come of their own accord because they recognize their needs are also accepted. In addition to the regular part time clinics held in cooperation with the county health departments, there is a full time, all purpose clinic established in Prince Georges County by the U. S. Public Health Service.

MICHIGAN

Annual Galen Lecture.—The 1948 annual lecture arranged by the Galen's Honorary Medical Society at the University of Michigan Medical School, Ann Arbor, was recently delivered by Dr. Stephen Rothman, professor of dermatology and syphilology, University of Chicago School of Medicine, on "Reactions of the Skin to Sunlight and Methods of Protection with Particular Reference to Para-Aminobenzoic Acid." Dr. Rothman spent one week at the university as visiting professor.

Final Checks from Kellogg Foundation.—The W. K. Kellogg Foundation is completing the plan on public health programs that it has underwritten since the early thirties in Allegan, Barry, Branch, Calhoun, Eaton, Hillsdale and Van Buren counties. Withdrawal has been spread over five years. Payments total $52,683.94 and bring to $2,455,091.27 the amount contributed by the foundation to establish and support local health departments. This support was part of the broad foundation program referred to as the Michigan Community Health Project. Field training programs for physicians, dentists, public health engineers, health educators and students in other fields will continue according to a second five year plan developed in 1947. A total of 1,394 persons have had field training experience in the seven counties in the training program to which the foundation has contributed $315,000 since 1933.

MINNESOTA

Johnston Lecture.—David P. C. Lloyd, Ph.D., Rockefeller Institute for Medical Research, New York, delivered the fourth annual John B. Johnston Lecture at the University of Minnesota Medical School, Minneapolis, May 19, on "Monosynaptic Reflexes and the Myostatic Unit." The lectures were established at the university in honor of the former dean of the college of science, literature and the arts, who died in 1939.

NEBRASKA

Memorial to Dr. Conlin.—At the annual meeting of the West Central Diabetes Association on March 16 a resolution was passed to establish a memorial award for the late Dr. Frank Conlin, its founder and first president. The award will be given annually for achievement in the field of diabetes. New officers elected at this meeting are all Omaha physicians: Morris Margolin, president; Charles R. Hankins, secretary, and Michael Crofoot, treasurer.

NEW MEXICO

Cancer Refresher Course.—One hundred and nineteen registrants, representing four states, were among the physicians and trained laymen who attended the refresher course on the diagnosis and treatment of cancer in Santa Fe April 15, sponsored by the New Mexico Division of the American Cancer Society, the Santa Fe County Medical Society and the Santa Fe Clinic, Inc. Among the speakers were: Drs. Roscoe R. Spencer, U.S. Public Health Service, Bethesda, Md.; Maurice N. Richter, New York, Herbert Willy Meyer, New York; Juan A. del Regato, Columbia, Mo., and Philip Rosenblum, Chicago.

Annual Meeting of State Medical Society.—The New Mexico Medical Society will hold its annual meeting at the Elks Club, Las Vegas, June 3-5 under the presidency of Dr. Victor K. Adams, Raton. Out of state speakers will be:

Jacob A. Bargen, Rochester, Minn., Management of Lesions of the Small Intestine.
Charles E. Shannon, Chicago, Injuries of the Head.
Morris Fishbein, Chicago, Editor, THE JOURNAL, Trends in Medical Legislation.
Fred Shapiro, Chicago, Intracapsular and Extracapsular Fractures of the Hip.
Earl E. Evert, Boston, Treatment of Cancer of the Bladder.
Arnold D. Tuttle, Chicago, Comfort Aloft.
William T. Carlisle, Chicago, Forewarning and Forearming in Obstetrics.
John A. Lichty, Denver, Rheumatic Fever.
H. H. Peterson, Chicago, Status of Socialized Medicine.

The annual dinner will be held Friday at 7:30 p.m. Dr. Fishbein will give the address on "The Medical Hucksters."

NEW YORK

Postgraduate Lecture—The Medical Society of the State of New York in cooperation with the New York State Department of Health has arranged a Postgraduate lecture for the Seneca County Medical Society at the Armitage Tea Room, Seneca Falls, May 27 at 2:30 p.m. Dr. Paul C. Clark, Syracuse, will speak on "Recent Advances in Therapeutics."

Emergency Service in Erie County.—Erie County has established a round the clock emergency medical service whereby an inquirer is given the telephone numbers of several physicians available at that particular hour when he cannot locate his own physician. In the first nineteen days of operation ninety-nine calls were handled, of which eighty-seven were classed as emergencies.

Establish Toxicology Division.—The University of Buffalo School of Medicine has established a toxicology division which will be supported jointly by the university and the County of Erie. The unit will work closely with city and county authorities, with hospitals and with industry in the determination of poisons. Director of the toxicology division is Dr. Niels C. Klendshoj, associate in pathology, working under Dr. Kornel Terplan, head of the department of pathology. Mr. Milton Feldstein, who had experience in this field at Bellevue Hospital, New York, and in the Army Sanitary Corps, was brought here to assist in this work. The Buffalo General and Meyer Memorial hospitals already have working arrangements with the laboratory, and efforts are under way to enlist the cooperation of other hospitals.

New York City

Dedicate Hospital Wing.—Dedication ceremonies were held for the $1,000,000 McNally Pavilion, a new wing of St. Clare's Hospital, April 18, making capacity of the hospital four hundred and forty-three beds. The wing is a memorial to Mr. and Mrs. Michael J. McNally and Miss Marguerite E. McNally, parents and sister of State Supreme Court Justice James B. McNally.

Dr. Woolley Receives Award.—The first research award of the American Pharmaceutical Manufacturers Association, which met in Havana, Cuba, April 12-17, was presented to Dilworth W. Woolley, Ph. D., aged 33, a blind associate member of the Rockefeller Institute. By his study of the antimetabolite of pellagra he has contributed to public health in those Latin American countries where pellagra has long been prevalent.

Annual Jones Lecture.—Sir Reginald Watson-Jones, British orthopedic surgeon, will deliver the eighteenth annual Sir Robert Jones Lecture at 8:30 p.m. Monday, May 24, at the Hospital for Joint Diseases on "Death and Growth of Bone." The lecture is part of a three-day Alumni Conference of the hospital, which will be held from May 24-26. Sir Reginald is the director of orthopedic and accident service of the London Hospital, London, as well as chief civilian consultant in orthopedic surgery to the Royal Air Force. The Jones lectures were established in 1930 in honor of the man who many consider the father of modern orthopedics. Sir Robert died in 1933.

Dr. Rousselot Appointed Clinical Professor.—Dr. Louis M. Rousselot, associate in surgery at Columbia University College of Physicians and Surgeons, has been appointed professor of clinical surgery at New York University College of Medicine and director of surgery at St. Vincent's Hospital. Dr. Rousselot will devote his full time as director of surgery at St. Vincent's Hospital, beginning August 1. Dr. Rousselot received his medical degree from Columbia University College of Physicians and Surgeons in 1927. He has been affiliated with Babies' Hospital since 1934, has been assistant attending surgeon at Presbyterian Hospital since 1938 and chief of the surgical clinic at Vanderbilt Clinic from 1939 to 1948.

Project to Study Job Ailments. — The Columbia University School of Public Health and Goodwill Industries of New York, Inc., have initiated research to help crippled persons by an accurate scientific analysis of their disability and the jobs they can do. The program will be set up at the "fatigue laboratory" in the workshop of Goodwill Industries. Columbia University will furnish physicians and nurses to conduct the program and will use it as a graduate training center. Dr. Leonard J. Goldwater, professor of industrial hygiene and director of instruction and research, said that all Columbia students in industrial medicine and the majority of the third year medical students in the College of Physicians and Surgeons will be assigned to Goodwill for instruction. The program was made possible by a gift of $25,000 from the Milbank Memorial Fund.

OREGON

State Health Council.—The Council of the Oregon State Medical Society at its meeting April 3 voted to sponsor an Oregon State Health Council and directed the Committee on Public Health, with Dr. Leslie S. Kent, Eugene, chairman, to make plans for its organization. Over a year ago the council issued a recommendation that all component societies assume the leadership in establishing countywide health councils. The Committee on Public Health will also assume responsibility for stimulating and assisting county council development. The Multnomah County Medical Society has sponsored a health council for nearly two years, and one is being organized in Malheur County, also under leadership of the county medical society.

PENNSYLVANIA

Fifty Year Practioners.—The first councilor district of the Medical Society of the State of Pennsylvania and the Woman's Auxiliary held a testimonial dinner May 19 to honor twenty-three physicians who have been in practice for fifty years. They are Oscar E. Boericke, Robert Boyer, Harry K. Carey, Frank A. Craig, George S. Crampton, John M. Cruice, Damaso deRivas, Harry M. Eberhard, Wilfred B. Fetterman, Charles R. Haig, Eugene T. Hinson, Henry C. F. Kellner, Richard W. Larer, Morris V. Leof, Catharine MacFarlane, Albert C. Menger, Charles F. Mitchel, George E. Pfahler, Herbert J. Smith, Stephen E. Tracy, George W. Truitt, Milton N. White and Nathaniel S. Yauger. Dr. Elmer Hess, Erie, president of the state medical society, made the presentations. The dinner address was given by Dr. Edward Bortz, Philadelphia, President of the American Medical Association, on "Mechanism and Humanism in Medicine."

Philadelphia

Cancer Hospital Dedicates Building.—The James Harvey Gravell Supervoltage Building, a part of the American Oncologic Hospital, was dedicated recently in Philadelphia. The building was presented to the hospital by Leon R. Cherksey, president of the American Chemical Paint Company, in memory of the late James Harvey Gravell, founder of the company. The reinforced concrete walls average 27 inches in thickness. The x-ray machine, capable of being stepped up to 5,000,000 volts, was presented at the same time by L. D. Cassett, retired Philadelphia businessman, in memory of his mother.

Books for War Devastated Countries.—The Association of Internes and Medical Students at Woman's Medical College of Pennsylvania has inaugurated a project of sending medical books and journals to war-devastated countries. They have sent 2,000 pounds (907 Kg.) to Prague, Czechoslovakia, to be distributed there through the Unitarian Service Committee or the International Students Union, and 2,000 pounds to China through the China Aid Council in New York. Used instruments are also urgently needed, as well as funds for drugs and vitamins. Any journals or used instruments sent to the Association of Internes and Medical Students at Woman's Medical College will be packed and shipped directly by the organization.

GENERAL

Group for the Advancement of Psychiatry.—About a hundred and fifty members of the American Psychiatric Association have organized a group for the advancement of psychiatry, and subcommittees have been appointed. For information write to Dr. Henry Brosin, Secretary, Group for the Advancement of Psychiatry, c/o University of Chicago, Chicago.

New England Health Institute.—The 1948 session of the New England Health Institute is to be held at the University of Massachusetts, Amherst, June 16-18, as a joint session with the Massachusetts Public Health Conference. University rooming and and dining facilities will be available to delegates from official and voluntary health agencies throughout the area.

Congress on Orthopaedic Surgery and Traumatology.—The Fourth Congress of the International Society of Orthopaedic Surgery and Traumatology will be held in Amsterdam, Netherlands, September 13-18. Speakers on the treatment of osteoarthritis of the hip include Padovani, France; Zahradnicek, Czechoslovakia; La Chapelle, Netherlands; Delchef, Belgium; Wiberg, Sweden; Mathieu, France, and Smith-Petersen, United States. Those discussing closed injuries to the spine are Nicoll, Great Britain; Bohler, Austria; Pais, Italy; Inclan, Cuba and San Ricart, Spain. Orthopedic surgeons in Europe at the time of the congress are invited and should notify Dr. J. Delchef, secretary general, Rue Montoyer 34, Bruxelles, Belgique; Dr. J.D. Mulder, secretary of the congress, Vondelstraat 75, Amsterdam, Pays-Bas, and Dr. Henry W. Meyerding, president of the congress, 102-110 Second Avenue, S.W., Rochester, so that hotel reservations may be made.

Special Libraries Association.—Major General Paul R. Hawley, U.S. Army Medical Corps, retired, former director of medical services of the Veterans Administration, will be the chief speaker at a luncheon of librarians in the biologic sciences and hospital and nursing librarians groups of the Special Libraries Association during the thirty-ninth annual convention of the association in Washington, D. C., June 6-12. Col. Joseph H. McNinch, Washington, D. C., director of the Army Medical Library, will be a guest at this meeting. At another joint meeting of the two groups on Thursday, June 10, Dr. Edward H. Cushing, Washington, D. C., will discuss "The Residency Program in Veterans Administration Hospitals."

Nutrition Awards.—At the annual dinner of the American Institute of Nutrition, Atlantic City, N. J., March 16, the following awards were made: 1. The Mead Johnson and Company Award for work on vitamin B complex was presented to Fritz Lipmann, Ph.D., Boston, head of the Biochemical Research Laboratory of Massachusetts General Hospital " for his work on the identification of pantothenic acid as a component of coenzyme A and to the recognition of its biochemical role in enzymatic acetylation and in the biological oxidation of acetic acid." Dr. Lipmann received the Carl Neuberg Medal of the American Society of European Chemists and Pharmacists for this same research contribution. 2. The Borden Award for distinctive research which has emphasized the nutritive significance of the components of milk or of dairy products was presented to Charles A. Cary, Riverdale, Md., chief, Division of Nutrition and Physiology, Bureau of Dairy Industry, U. S. Department of Agriculture, for his " research concerning the influence of diet on the composition of blood and milk constituents; occurrence and losses of carotene in roughage; vitamin A potency of milk and butter and the relation of same to the quality of roughage; unidentified nutrients necessary for normal growth which are found in milk and milk products, and in certain other foods and feeds."

Society for Vascular Surgery.—The Society for Vascular Surgery will hold its second annual meeting June 20 at the Stevens Hotel, Chicago, under the presidency of Dr. Arthur W. Allen, Boston. The program includes:

Arthur W. Allen, Boston, Venous Thrombosis and Pulmonary Embolism.
John Homans, Boston, Venous Thrombosis in the Lower Limbs.
Michael E. DeBakey and E. W. Alton Ochsner, New Orleans, Gangrene as a Complication of Thrombophlebitis.
Claude S. Beck, Cleveland, Revascularization of the Heart.
Geza de Takats, Chicago, Corticoadrenal Factor in Essential Hypertension.
Herman E. Pearse, Rochester, N. Y., Cellulose and Cellophane Products in Vascular Surgery.
Daniel C. Elkin and Frederick W. Cooper Jr., Atlanta, Ga., Radioactive Isotopes in the Investigation of Vascular Disease.
Ross Veal, Washington, D.C., Surgical Treatment of Hyperhidrosis.
Frederick A. Coller, Kenneth N. Campbell, and Robert E. L. Berry, Ann Arbor, Mich. and Bradley M. Harris, Ypsilanti, Mich., Lumbar Sympathectomy in Advanced Arteriosclerosis Obliterans.
Reginald H. Smithwick and George P. Whitelaw, Boston, Effect of Sympathectomy on Heart Rate.
Louis G. Herrmann and Joseph A. Buchman, Cincinnati, Complications from Injuries to Arteries.
Arthur H. Blakemore, New York, Portacaval Anastomosis for Portal Hypertension.
I. Hiss Gage, New Orleans, Cardiac Decompensation Secondary to Arteriovenous Fistula.
Norman E. Freeman, San Francisco, A Technic for Division and Suture of the Patent Ductus Arteriosus.
Robert H. Linton, Brookline, Mass., Treatment of Arteriosclerotic Popliteal Aneurysm.

Report of Interim Commission.—At the fifth session of the World Health Organization Interim Commission in Geneva, Switzerland, January 22-February 7, the report on the activities of the commission since its establishment at the International Health Conference in New York in 1946 was approved for submission to the World Health Assembly in Geneva June 24 - July 31. The proposed 1949 budget for the World Health Organization amounts to $6,367,995, of which $1,071,690 is allotted for fellowships, medical literature, teaching equipment and emergency medical supplies. Major recommendations by the commission to the first World Health Assembly and W.H.O. include the following: (1) Continuation of medical cooperation with accredited governmental and nongovernmental agencies. It recommends that the World Health Organization serve in an advisory capacity in the fields of public health and medicine with the International Civil Service Advisory Board, the United Nations Social Commission, the U. N. Scientific Conference for the Conservation and Utilization of Resources, International Labor Organization United Nations Educational, Scientific Cultural Organization. It recommended that aid be continued to the International Children's Emergency Fund in launching an antivenereal campaign among children and women through mass treatment with penicillin; (2) Continuation of the epidemologic service and revision of existing sanitary conventions; (3) continuation of the work of biologic standardization and unification of pharmacopeias, (4) creation of an international influenza center, which is now well under way; (5) revision of the international lists of diseases and causes of death; (6) appointment of a designated representative of countries not having a scientific attaché in the United States for distribution of radioactive isotopes by the United States; (7) promotion of health protection for children; (8) programs of malaria, tuberculosis and venereal disease control, and maternal and child health; (9) continuation of field services and medical mission sent under UNRA to various countries.

Marriages

ALBERT HEWETT COONS, Boston, to Miss Phyllis E. F. Watts of Milton in December 1947.

FORREST CLARENCE ORMAN, Roanoke, Va., to Miss Mary Virginia Leonard of Galax, Dec. 6, 1947.

JOHN E. OOTTSCH, Shenandoah , Iowa to Miss Rachel E. Updegraff of Sigourney in New Orleans, January 31.

CORRECTIONS

Preliminary Program of Scientific Assembly—In THE JOURNAL, May 15, in the program of the Section on Ophthalmology, Wednesday, June 23, the title of the fourth paper, by Theodore H. Ingalls, "Epidemiology of Encephalo-Ophthalmic Dysplasia," was omitted; in the program of the Section on Pediatrics, June 23, the last name among the authors of the fourth paper should be "Herman" not "Herbert" N. Bundesen; in the Section on Pathology and Physiology, Friday, June 25, the authors of next to the last paper should have read: "Lester M. Morrison, Lillian M. Hall, Albert L. Chaney and William Gonzales."; in the Section on Gastro-Enterology and Proctology, June 23, the name of one of the authors of the last paper should have been "D. F. Richfield" instead of "Richkield;" in the Section on Miscellaneous Topics, Session on Physical Medicine, the third paper to be presented in the Panel Discussion on "Physical Treatment of Poliomyelitis" by Robert L? Bennett, Warm Springs, Ga., was omitted.

Deaths

Hill Hastings ● Los Angeles; born in Elizabethtown, Ky., Jan. 9, 1874; University of Virginia Department of Medicine, Charlottesville, 1895; an Affiliate Fellow and in 1915-1916 chairman, Section on Laryngology, Otology and Rhinology of the American Medical Association; emeritus professor of surgery (otology, rhinology and laryngology), University of Southern California School of Medicine; member and formerly vice president of the American Laryngological Association; member and past president of the Los Angeles Society of Oto-Laryngology and the American Laryngological, Rhinological and Otological Society; member of the Pacific Coast Oto-Ophthalmological Society; assistant surgeon, U.S. Public Health Service, from 1897 to 1902; captain in the medical corps of the U.S. Army during World War I; affiliated with Los Angeles County General Hospital, Children's Hospital and the Good Samaritan Hospital, where he died February 14, aged 74, of bronchopneumonia.

William Lowndes Peple ● Richmond, Va.; born in Manchester, Va., Dec. 5, 1875; University College of Medicine, Richmond, 1897; emeritus professor of clinical surgery at the Medical College of Virginia; member of the founders' group of the American Board of Surgery; member and formerly vice president of the Southern Surgical Association and of the Medical Society of Virginia; fellow of the American College of Surgeons; past president of the Richmond Academy of Medicine and the Tri-State Medical Association; served in France during World War I; for many years associated with St. Luke's Hospital; died February 7, aged 73, of cerebral hemorrhage.

Fred Franklin Attix ● Lewistown, Mont.; born in Detroit Lake, Minn., Aug. 8, 1878; University of Pennsylvania Department of Medicine, Philadelphia, 1900; past president of the Montana State Medical Association; member and formerly vice president of Western Surgical Association; member of the American Association for the Surgery of Trauma and the Radiological Society of North America, Inc.; member of the founders' group of the American Board of Surgery; president of staff, St. Joseph's Hospital; founder and president, Attix Private Clinic Hospital; district surgeon, Chicago, Milwaukee, St. Paul and Pacific Railroads; died February 9, aged 69;

Harry Kraylor Born ● Los Angeles; born in Indianapolis, Aug. 9, 1886; Indiana University School of Medicine, Indianapolis, 1908; associate clinical professor of surgery at the College of Medical Evangelists; member of the founders' group of the American Board of Surgery; member of the Western Surgical Association; fellow of the American College of Surgeons; affiliated with Presbyterian Hospital-Olmsted Memorial; attending surgeon, Los Angeles County Hospital and member of the senior staff of the California Hospital; died in the Methodist Hospital February 8, aged 61, of cerebral hemorrhage and essential hypertension.

Louis Abraham Feldman ● Brooklyn; born in Brooklyn in 1890; University and Bellevue Hospital Medical College, New York, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; formerly affiliated with the Indian Service in White Earth, Minn.; fellow of the American College of Surgeons; affiliated with the Brooklyn Hebrew Home and Hospital for Aged and the Jewish Hospital; attending ophthalmologist to Sea View Hospital, Staten Island; died in Palm Beach, Fla., February 2, aged 57, of cerebral hemorrhage.

Alfred Franklin Hocker ● New York; born in Audubon, Iowa, April 29, 1902; University of Louisville (Ky.) School of Medicine, 1926; assistant professor of radiology at the Cornell University Medical College; specialist certified by the American Board of Radiology, Inc.; member of the American College of Radiology and the American Radium Society; director of the tumor clinic at the Cornwall (N.Y.) Hospital; on the staffs of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York Hospital and the White Plains (N.Y.) Hospital; died February 12, aged 45, of coronary thrombosis.

Isaac Spencer Finney Dodd ● Pittsfield, Mass.; born in Hangchow, China, Feb. 20, 1868; University of the City of New York Medical Department, New York, 1890; member of the founders' group of the American Board of Surgery; fellow of the American College of Surgeons; past president of the Berkshire District Medical Society; served during World War I; on the staff of the Fairview Hospital in Great Barrington, House of Mercy and St. Luke's Hospital; died in the Palmer Memorial Hospital, Boston, January 30, aged 79, of carcinoma of the colon.

John Wilson Poucher, Poughkeepsie, N.Y.; born in Claverack, N.Y., July 24, 1859; Albany (N.Y.) Medical College, 1883; instrumental in the organization of the Dutchess-Putnam Medical Society, which he served as president; fellow of the American College of Surgeons; veteran of the Spanish-American War; for many years affiliated with the Vassar and St. Francis hospitals; served as manager and president of the board of the Hudson River State Hospital; for many years secretary of the Dutchess County Historical Society; died February 16, aged 88, of arteriosclerosis.

Frank E. Andrews, Norfolk, Va.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1904; found dead February 18, aged 80.

Francis Richard Anthony, Maryville, Mo.; Missouri Medical College, St. Louis, 1898; member of the American Medical Association and in 1907 member of its House of Delegates; past president of the Nodaway County Medical Society; died in St. Francis Hospital February 16, aged 75, of a hip fracture received in a fall.

Glenn Wyatt Arthurs, Niagara Falls, N.Y.; University of Buffalo School of Medicine, 1918; member of the American Medical Association; served during World War I; on the staffs of the Memorial and Mount St. Mary's hospitals; died February 10, aged 52, of coronary thrombosis.

Lewis Harlan Athon, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; member of the American Medical Association; on the staff of the Methodist Hospital; died February 26, aged 60, of carcinoma.

Harold Woods Baker, Orford, N.H.; Harvard Medical School, Boston, 1906; fellow of the American College of Surgeons; at one time an assistant at the Mayo Clinic in Rochester, Minn.; served on the faculty of his alma mater and on the staffs of the Charlesgate Hospital in Cambridge, Mass., and the Free Hospital for Women in Brookline, Mass.; died February 14, aged 66, of hypertension and cerebral thrombosis.

Irving Sydnor Barksdale, Greenville, S.C.; Yale University School of Medicine, New Haven, 1923; member of the American Medical Association; at one time on the faculty of the Medical College of the State of South Carolina in Charleston; for many years city health officer; died in St. Francis Hospital February 10, aged 50, of cerebral hemorrhage.

Julius Peter Karp, Hartford, Conn.; Maryland Medical College, Baltimore, 1913; Kansas City College of Medicine and Surgery, 1917; died in the Hartford Hospital February 14, aged 69, of coronary disease.

Felix Max Katar, Philadelphia; Maryland Medical College, Baltimore, 1910; member of the American Medical Association; died Dec. 7, 1947, aged 77, of coronary sclerosis.

Joseph Adelbert Keithley, Palmyra, Wis.; Illinois Medical College, Chicago, 1902; past president of the Jefferson County Medical Society; served during World War I; died in Lakeland, Fla., January 15, aged 73, of coronary thrombosis.

Arthur Edward Lamley ● Blissfield, Mich.; Medico-Chirurgical College of Philadelphia, 1909; served as health officer and county coroner; died in Bixby Hospital, Adrian, February 10, aged 62, of primary atypical pneumonia.

Erwin Last ● New York; Universität Bern Medizinische Fakultät, Switzerland, 1919; member of the New York Post Graduate Hospital; died February 12, aged 52, of coronary thrombosis.

Eugene Joseph Leopold ● Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1905; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; on the staffs of the Johns Hopkins and Sinai hospitals; died January 14, aged 68.

Emry Franklin Lewis, Ada, Okla. (licensed in Oklahoma under the Act of 1908); died January 13, aged 82.

Philip A. Ley, Donora, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1904; also a graduate in pharmacy; member of the American Medical Association; served as school director, member of the board of health and medical examiner for the public schools; died February 5, aged 68, of carcinoma of the liver.

Walter Mathews Lott ● Nashville, Tenn.; Emory University School of Medicine, Atlanta, 1918; served during World War I; died February 15, aged 53, of carcinoma of the stomach.

William Barker McCreery ● Tacoma, Wash.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; fellow of the American College of Surgeons; on the staffs of the Tacoma General and St. Joseph's hospitals; died Dec. 28, 1947, aged 73, of coronary disease.

Wilbur Washington Mackenzie, Los Angeles; College of Physicians and Surgeons, Chicago, 1896; fellow of the American College of Surgeons; died recently, aged 78.

John M. Meadows, Vidalia, Ga.; University of Georgia Medical Department, Augusta, 1888; member of the American Medical Association; died January 22, aged 86.

Walter McDonald Merritt, Boyle, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1906; member of the American Medical Association; served during World War I; formerly assistant superintendent of the State Insane Hospital, Asylum; died in Baptist Hospital, Memphis, Tenn., February 1, aged 65, of heart disease.

Joseph Bonnedick Metzger, Toledo, Ohio; Ohio State University College of Medicine, Columbus, 1915; member of the staff of St. Vincent's Hospital; died January 24, aged 64.

David G. Miller, Doraville, Ga.; University of Georgia Medical Department, Augusta, 1887; died January 20, aged 84.

F. A. Minnis, Phoenix, Ariz.; Tennessee Medical College, Knoxville, 1907; died in the Good Samaritan Hospital February 7, aged 74.

Robert Sterling Montgomery ● South Hill, Va.; Medical College of Virginia, Richmond, 1934; physician to the Selective Service Board during World War II; died February 9, aged 37, of amyotrophic lateral sclerosis

Julia Morgan, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1920; diplomate of the National Board of Medical Examiners; associate in medicine at her alma mater formerly a medical missionary in China, where she was on the faculty of the Cheeloo University School of Medicine, Tsinan, Shantung; received the honorary degree of doctor of science from Dickinson College, Carlisle, Pa.; died in the University of Pennsylvania Hospital January 26, aged 56, of coronary sclerosis.

Thomas Morgan, Alton, Ill.; Baltimore Medical College, 1895; died in St. Joseph's Hospital February 1, aged 76, of injuries received when struck by an automobile while he was crossing the street.

Ernest Mosby, Waynesboro, Va.; Medical College of Virginia, Richmond, 1899; died February 5, aged 71.

William Archibald Murray, Scranton, Pa.; Jefferson Medical College of Philadelphia, 1929; member of the American Medical Association; affiliated with Mercy Hospital, where he died February 14, aged 53, of heart disease.

Sverre Oftedal ● Glendale, Calif.; Rush Medical College, Chicago, 1911; fellow of the American College of Surgeons; on the staff of the Physicians and Surgeons Hospital; died February 4, aged 64.

Francis Michael Pare, Worcester, Mass.; Georgetown University School of Medicine, Washington, D.C., 1931; member of the New England Obstetrical and Gynecological Society and the American Medical Association; affiliated with St. Vincent's Hospital, where he died January 28, aged 45, of lymphoblastoma.

Ralph Wait Parsons, Seattle; College of Physicians and Surgeons, medical department of Columbia College, New York, 1890; at one time physician in charge of the Greenmont-on-the-Hudson in Ossining, N.Y., where he practiced medicine and was a member of the library board; died January 29, aged 80, of carcinoma of the prostate.

Judson Philbrook Pendleton ● Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1898; fellow of the American College of Physicians; past president of the Brooklyn Pediatric Society; affiliated with the Coney Island, Kingston Avenue, Cumberland Street and Methodist hospitals; died January 21, aged 74.

Anthony Salvatore Pendola, Holyoke Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1920; member of the American Medical Association; served during World War I; formerly assistant physician affiliated with the Providence and Holyoke hospitals; died January 10, aged 57, of carcinoma.

Clarence George Perry, St. Paul; University of Minnesota College of Medicine and Surgery, Minneapolis, 1909; member of the American Medical Association; served during World War I; died in Pharr, Texas, January 6, aged 62, of coronary occlusion.

Thomas Adolphus Peterson ● Wynne, Ark.; University of Tennessee College of Medicine, Memphis, 1932; died February 3, aged 40.

Harold Ashton Pingree, Portland, Maine; Medical School of Maine, Portland, 1901; member of the American Medical Association; formerly on the faculty of his alma mater; fellow of the American College of Surgeons; served with the U. S. Public Health Service; affiliated with the Maine General and Children's hospitals; died January 7, aged 70, of heart disease.

Eva Prescott, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; died February 3, aged 71.

Arthur Augustus Rankin, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1900; died in the Fairview Hospital January 4, aged 75, of a rupture of the left cardiac ventricle.

Maten Floyd Rathbun, Hanover, Ill.; Chicago Medical School, 1921; served during World War I; died January 25, aged 53.

Frederick Bonga Rawlings ● Sandersville, Ga., University of Pennsylvania School of Medicine, Philadelphia, 1915; member of the Southeastern Surgical Congress and the Southern Medical Association; past president of the Washington County Medical Society; fellow of the American College of Surgeons; served overseas with the Emory Unit during World War I; senior surgeon of Rawlings Sanitarium; died in the Emory University Hospital, Atlanta, January 16, aged 58, of carcinoma of the pancreas.

Claude Everett Richmond ● Colorado Springs, Colo.; Barnes Medical College, St. Louis, 1909; past president of the El Paso County Medical Society; specialist certified by the American Board of Anesthesiology, Inc.; member of the American Society of Anesthesiology; affiliated with the Glockner-Penrose Hospital, Memorial Hospital and the St. Francis Hospital and Sanatorium; died February 4, aged 60, of coronary thrombosis.

Ralph Weller Rucker, Bartlesville, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1936; member of the American Medical Association; specialist certified by the American Board of Otolaryngology; past president of the Washington-Nowata Counties Medical Society; served during World War II; died in Norman January 27, aged 37, of injury received in a fall.

Emil Albin Rundquist ● New York; Columbia University College of Physicians and Surgeons, New York, 1898; fellow of the American College of Surgeons; formerly on the faculty of the New York Post-Graduate Medical School and Hospital, Columbia University; died in January, aged 72.

Charles Morehead Smith, Dixon, Ky.; Missouri Medical College, St. Louis, 1885; member of the American Medical Association; secretary of the Webster County Medical Society; for many years health officer of Webster County; died in the Vanderbilt Hospital, Nashville, Tenn., January 28, aged 84, following an operation for cholelithiasis.

Herbert Lee Sproul, Waverly, N.Y.; Long Island College Hospital, Brooklyn, 1895; died January 25, aged 70, of arteriosclerotic heart disease.

Fred Wilson Standefer ● Lubbock, Texas; University of Texas School of Medicine, Galveston, 1917; served overseas during World War I; associated with the West Texas Hospital and Clinic; died January 22, aged 54, of heart disease.

Gordon Livingston Todd, Princeton, W. Va.; University of Virginia Department of Medicine, Charlottesville, 1910; member of the American Medical Association; fellow of the American College of Surgeons; owner and medical director of the Mercer Memorial Hospital; died February 3, aged 53, of heart disease.

Thomas Tilghman Tolson, Longstreet, La.; Chicago College of Medicine and Surgery, 1914; died at the Tri-State Hospital in Shreveport January 22, aged 57.

William Porter Verity, Two Buttes, Colo.; Rush Medical College, Chicago, 1879; member of the American Medical Association; for many years county coroner; died in the Sacred Heart Hospital, Lamar, January 13, aged 94.

Paul Henry von Zierolshofen ● Croghan, N. Y.; University of the City of New York Medical Department, New York, 1887; served during World War I; for many years fire chief; affiliated with the Lewis County Hospital in Lowville and St. Lawrence State Hospital in Ogdensburg; vice president of the Croghan National Bank; died January 20, aged 84, of coronary occlusion.

John A. Waggener, Humboldt, Neb.; Louisville (Ky.) Medical College, 1876; member of the American Medical Association; past president of the Richardson County Medical Society; served as county coroner; died January 23, aged 95.

John Edward Walton ● Alton, Ill.; Marion-Sims College of Medicine, St. Louis, 1897; past president of the Madison County Medical Society; member and formerly chief of staff, Alton Memorial Hospital; served during World War I; died January 25, aged 80, of coronary occlusion.

Philip Carter Washburn, Morris Plains, N. J.; Columbia University College of Physicians and Surgeons, New York, 1900; an officer during World War I; for many years on the staff of the New Jersey State Hospital at Greystone Park; formerly on the staffs of the Manhattan and Kings Park State hospitals in New York; died January 10, aged 72, of coronary thrombosis.

John Cowden Welch, Bellevue, Pa.; Medico-Chirurgical College of Philadelphia, 1893; district registrar of vital statistics; founder and original staff member of St. John's General Hospital in Pittsburgh; affiliated with the Suburban General Hospital, where he died February 3, aged 80, of cerebral thrombosis and diabetes mellitus.

Benjamin Franklin Williams, Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1910; died January 8, aged 64.

Millard Lewis Wilson, Falls City, Neb.; Lincoln Medical College of Cotner University, 1896; member of the American Medical Association; served as mayor of Humboldt, as coroner and health officer of Richardson County; affiliated with Our Lady of Perpetual Help Hospital, where he died January 28, aged 80, of acute gangrenous appendicitis.

Charles F. Wixom, North Cohocton, N. Y.; University of Buffalo School of Medicine, 1892; died in the Wayland (N.Y.) Hospital January 20, aged 88, of arteriosclerosis.

John George Wurts ● Philadelphia; Hahnemann Medical College and Hospital, Philadelphia, 1907, and Jefferson Medical College of Philadelphia, 1908; specialist certified by the American Board of Pathology, Inc.; member of the American Society of Clinical Pathologists; affiliated with the Women's Homeopathic Hospital, where he died January 15, aged 62, of cerebral hemorrhage.

Foreign Letters

LONDON

(From Our Regular Correspondent)

April 16, 1948.

Blood Transfusion Service for London Hospitals

During and since the war blood transfusion has greatly developed and services have been organized all over the country. The Greater London Blood Transfusion Service, which covers London and five adjoining counties, serves fifty hospitals. The service is responsible for the supply of donors in cases in which freshly drawn blood is essential. Every call is for a definite patient (there is no blood bank), and therefore the urgency of the demand is brought home to the donor. As the service has become known, the number of calls has increased. There were 1,095 requests in 1945, 1,863 in 1946 and 2,436 in 1947. In January 1948 the number was 273. The most received in any one day was 27.

On enrollment, donors undergo medical examination, their blood is tested and grouped by the medical officer of the service, Dr. H. F. Brewer, at the pathologic department, St. Bartholomew's Hospital. The service can supply not only Rh-negative and Rh-positive donors of the A, B, AB and O groups but also donors of the rare Rh subgroups for both transfusion and research purposes. No maximum is fixed for any one donor. More than half have given blood over ten times, and more than a fourth over twenty times. One donor has served more than one hundred times, and the seventieth birthday of another was celebrated by the seventieth transfusion, though 65 is the usual age limit. The minimum period between donations is three months for men and four months for women. In only 2 of 60,000 cases has the service learned that the donor's health has suffered temporarily from the donation. But all donors are insured against ill effects and are examined after the completion of each ten transfusions. The donors are not paid for their services but are reimbursed for their expenses.

Cardiac Catheterization

At a joint meeting of the Manchester Medical and Pathological Societies Professor J. McMichael lectured on cardiac catheterization, which was introduced by Forssman in 1929. Subsequently it was used extensively in Portugal, France and Latin America to inject radiopaque substances so as to define vessels at the root of the lung. In 1941 Cournand described its use for measuring pressure in the chambers of the heart and for measuring the cardiac output by the Fick principle. Use of the method in the London Postgraduate School has been without untoward incident in 800 cases and is now spreading widely. Blood never clots on the surface of the catheter, but small pinhead thrombi occasionally form on the tip, and some may escape into the lungs, where there is good reason to believe that they are harmless. In the right ventricle the tip may excite extrasystoles, which may be harmful to patients whose cardiac condition is precarious. One death has been reported in the Netherlands in a case of gross coronary disease.

In congenital heart disease the simpler defects may often be diagnosed by cardiac catheterization. A defect of the interauricular septum is recognized by the admixture in the right auricle of arterial and venous blood. But the selection of cases for Blalock's operation is usually made on clinical grounds. Bing's recent success in sampling blood from the coronary sinus has opened possibilities. Cardiac catheterization has come to stay.

Precautions Against Harmful Results of Atomic Research

An establishment for research on atomic energy has been installed at Harwell, on the Thames, by the government. Precautions have been taken, on the advice of the Medical Research Council's research committee on the medical and biologic application of nuclear physics, to insure that the water used is returned to the Thames free from the risk of harmful radioactivity. A certain amount of radioactivity in drinking water can be tolerated by human beings, and the Medical Research Council has laid down a tolerance for Thames water such that the effects of consumption will be negligible. About a million gallons of water will be used daily at the research station. Most of it will be for cooling plant and domestic needs. The rest will be for research purposes, some of them radioactive. A carefully controlled water system will be installed. The most highly active portion of the water will be segregated and withheld from the river. The remainder will be passed to storage tanks, where it will be (1) tested by medical officers for compliance with the agreed tolerances, (2) treated for chemical impurities, and then (3) mixed with the domestic water before being discharged into the Thames.

The system of treatment and examination has been so devised that several operations have to be carried out before the water is discharged. A new weir is being constructed at the point of discharge so that the water will be turbulently mixed with much greater quantities of river water before it joins the main stream. These safeguards have received the approval of the Ministry of Health.

Orthopedic Surgery in Rheumatiod Arthritis

At the Section of Physical Medicine of the Royal Society of Medicine Mr. A. W. Law opened a discussion on orthopedic surgery in rheumatoid arthritis and ankylosing spondylitis. He had lately spent some months at the Massachusetts General Hospital studying the methods of Bauer and Smith Petersen. He said that the orthopedic surgeon is taking a greater share in overcoming the deformities of these diseases. The team work of a physician, an expert in physical medicine and an orthopedic surgeon is necessary, and in certain cases high voltage roentgen therapy may also be required. The principle of rest is still the basis of the so-called conservative treatment of rheumatoid arthritis, but it may be harmful from the point of view of restoration of function. A careful balance must be preserved between rest and active exercise, pain being controlled if necessary by drugs. In many rheumatoid cases multiple deformities necessitate a long program of reconstructive or functional treatment. One or more revision operations may be necessary for a satisfactory end result.

Taking first the upper limb, a painful shoulder joint with deformity of adduction and internal rotation is frequent. Excision of the acromion process, with removal of subacromial bursae, eliminates the source of pain and allows free movement. Relief of pain helps to remove muscular spasm. In rheumatoid arthritis of the elbow spasm of the biceps is prominent. Smith Petersen has shown that the radial head may be drawn upward so as to impinge on the capitellum. Excision of the radial head overcomes such faulty joint mechanics, pain is relieved and a considerable improvement in

range is obtained. When there is gross destruction or complete ankylosis excision of the lower end of the humerus and upper ends of the radius and ulna is indicated. The hip and knee joints frequently require surgical treatment on account of pain and deformity with a variable degree of ankylosis. When the patient's morale is low and the muscles wasted and fibrotic a stabilizing process such as athrodesis may be useful. The problem of bilateral stiff hips and knees may have to be faced. A reconstructive operation before fibrosis of muscles and joints has progressed too far should be performed. The technic of Smith Petersen's arthroplasty of the hip, to create all the elements of the joint, has been greatly improved by the use of the "vitallium" mold, which becomes a barrier to recurring ankylosis. Any reconstruction of the hip joint must produce a joint which is painless, stable and capable of bearing weight.

Eire Doctors Reject a State Medical Service

Evidently as a result of the British proposal, the question of a state medical service has been raised in Irish politics. A special meeting of the Medical Association of Eire has been held to discuss the White Paper on the Eire Health Act of 1947. The meeting unanimously passed the following resolutions: (1) that many of the provisions of the health act of 1947, as outlined in the White Paper, are unworkable, and (2) that the central council of the Medical Association of Eire is opposed to the taking over or direction by the state of all medical services and to the degree of state control and direction that is visualized.

Experimental Psychology: A New Journal

Increasing interest in experimental pathology has led the Experimental Psychology Group to found a new journal, the *Quarterly Journal of Experimental Psychology*. Editorial inquiries should be addressed to Mr. R. C. Oldfield, M.A., Institute of Experimental Psychology, 34 Banbury Road, Oxford, England. The Journal may be ordered, 7½ s. annually or 2 s. per issue, from W. Heffer & Sons, Ltd., 3-4 Petty Cury, Cambridge, England.

Dentists Reject National Health Service

The British Dental Association announces that the decision of the representative board to recommend members not to enter the National Health Service has been followed by meetings of nine branches at which 1,080 votes were cast against any participation in the service and only 33 in favor of entering it.

ANKARA

(From Our Regular Correspondent)

March 12, 1948

Folic Acid Therapy

A sample of folic acid came to Turkey late in 1946, and Professors Tevfik Saglam and E. Frank, of Istanbul University Hospital, were the first to apply it with excellent results in cases of pernicious anemia.

A patient was given a daily dose of four tablets of folic acid but no liver extract. Reticulocytes, which before treatment had been subnormal, increased to 18 within a week; red blood cells and hemoglobin began to increase accordingly, and the whole blood picture gradually changed. Within eighteen days the red blood cell count rose to 3,850,000, with hemoglobin 68 per cent. After that the patient was given iron and ascorbic acid. A week later the red blood cell count rose to 4,000,000, the hemoglobin level to 72 per cent. The second sternal puncture revealed a decrease of megaloblasts from 30 to 4.5. In the third myelogram on the twenty-ninth day of treatment, megaloblasts had completely disappeared. The number of white blood cells, which before treatment amounted to only 3,000, gradually increased to 7,000 with a resultant great improvement in the patient's health and disappearance of the pains. This had been attained with 500 mg. of folic acid.

Half Century of Children's Hospital

As a memorial to his beloved daughter, the Sultana Hadidche, who died of diphtheria at 10 years of age, Sultan Abdul Hamid II established the Istanbul Children's Hospital, which was opened in 1898. It had six pavilions with steam heat, one hundred beds, and was erected at the cost of 40,000 pounds Turkish in gold. Ibrahim pasha, who had been in attendance when the sultana died, was appointed physician in chief. This, the only children's hospital in Istanbul, has during the republic (since 1923) been remodeled. Today it has three hundred beds and departments for every speciality. More than 100,000 persons a year come to the outpatient department. In 1933 Istanbul University was reorganized and the children's hospital became part of it, the department of pediatrics, orthopedics and urology serving as a teaching center for medical students. At present only the department of pediatrics, which is under the direction of Professor Ihsan Hilmi Alantar, serves that purpose. As soon as the children's hospital of the university is finished, it will cease to be a teaching hospital. Two years ago the Ministry of Health added a new building, a nurses' home and a training school for hospital and public health nurses. There are at present one hundred students. The course lasts three years. Under the ten year National Health Plan seven three hundred bed children's hospitals are to be erected in the principal cities and towns.

Infantile Kala-Azar

At the monthly meeting of the Istanbul Medical Society Dr. N. M. Fakecelli of the Austrian Saint George Hospital, Istanbul, reported a case of kala-azar in an infant 13 months of age. According to the mother, who lived in Istanbul on the Bosporus, the onset of fever, lack of appetite, increasing weakness and swelling of the abdomen began four months prior to the child's admission at the hospital in September 1947. Because of the mother's illness, breast feeding had been discontinued after seven months, and the child was fed cow's milk. Plasmodia were not present in the blood smear; coagulation of the blood was normal. Sternal puncture was made the next day, and leishmania were found in splenogram and myelogram. Because the child was in a critical condition and ethylstibamine ("neostibosan") was not available, antimony and potassium tartrate had to be resorted to. A blood transfusion of 30 cc. was given by the father; iron and vitamin preparations were administered. The child died of pneumonia on the seventeenth hospital day.

Dr. Fakecelli discussed the 39 cases of kala-azar which had come to his clinic in the last nine years. He said that the formolgel test, Gate and Papacostas tests are a great help in arriving at the diagnosis, but they should not be relied on solely. The tests had been positive in 34 of 39

cases, and undecided in 5. The most reliable method to arrive at a true diagnosis was to search for and locate the parasites in the spleen and bone marrow. In 2 of 18 cases in which parasites had not been found either in the myelogram or the splenogram, an abundance of leishmania had been found in the spleen. Though in the myelogram of 16 patients there had been only a few Leishmania, there were an abundance in the spleen, indicating that the safest method is the splenic puncture. Of 34 patients who every other day received an intravenous injection of "neostibosan," 31 patients recovered. Because "neostibosan" was not available antimony and potassium tartrate had to be resorted to for 6 patients, of whom 3 recovered and 3 died. All 39 patients had come from the Golden Horn and the Bosporus, indicating that in these regions kala-azar is endemic and requires precautionary measures.

PARIS

(From Our Regular Correspondent)

March 30, 1948.

Blood Transfusion Centers

A new order of the Ministry for Public Health and Population pertains to blood transfusion centers. Regional centers are under the management of a director assisted by a committee consisting of nine members: (1) a specialist in blood transfusion; (2) a hematologist; (3) a dermatologist; (4) an obstetrician; (5) a surgeon; (6) a representative of blood donors; (7) a representative of the Regional Social Security Fund; (8) a representative of public or private collectives, and (9) a representative of the Syndicate of Doctors. Centers have to insure a supply of preserved blood, fluid or dry plasma, and convalescent serum to medical establishments and district transfusion centers. Regional centers will also take part in scientific research and in the education of the medical corps with regard to blood transfusion; they will cooperate with the National Institute for Hygiene. District centers under the management of public or private collectives will have a consultative committee of six members, and they will assume the recruiting of blood donors and the institution of emergency blood transfusion services.

The national center for blood transfusion is the oldest in the world, having been created in 1923 by Professor A. Tzank, the present director, and by Professors Levy-Sclal and Gosset. Located in an annex of the St. Antoine Hospital, its activities embrace arm to arm transfusions, the preparation of plasma and preserved blood, the control of reactions to transfusions, the registration of future donors and the participation in the organization of regional and departmental centers. To those actitivities add also collaboration with the Percy Hospital Army Transfusion Center. Its official paper is the monthly *Revue d' hematologie.*

Research at the National Center.—Research is progressing in various directions in the Laboratory of the National Center. Caroli and Bessis' research on hereditary erythroblastosis opens a large field of experimentation in human serology and has great scientific and practical value. Bessis and Bernard, who use the exchange transfusion in the treatment of acute leukemia, in collaboration with Buhot have perfected the technic using Diamond's catheter. After exposing a vein at the elbow, the catheter is introduced up to the venous confluent at the base of the neck. Then the blood exchange is performed by means of the two way syringe (Tzank's type). They believe this method may be applied also in the treatment of intoxications when the poison is still in the blood and the anatomic lesions are not irreversible. Research is in progress to ascertain whether the effective substances in normal blood are carried by the corpuscles, or, if by the plasma, by what fraction of the plasma. The experiments of these and other workers show that in acute leukemia exchange transfusion only produces recovery exceptionally but in all cases prolongs the patient's life. Tzank and Andre have studied post-transfusion reactions in a series of 6,000 transfusions. They conclude that a previous injection of morphine diminishes the frequency of such reactions and that transfusions without anesthesia are practically never followed by accidents. Post-transfusion reactions occur in 15 per cent of cases. While these reactions have no relation to the rapidity of the injection, Tzank and Andre recommend that the first 30 to 40 cc. of blood be injected slowly.

RIO DE JANEIRO

(From Our Regular Correspondent)

April 9, 1948.

New Pathogenic Concept of American Trypanosomiasis

Drs. Julio Muniz and A. Penna de Azevedo, of the Oswaldo Cruz Institute, Rio de Janeiro, published a paper describing their investigation of the action of Tripanosoma cruzi, causative agent of the American trypanosomiasis, on man. Their main objective was to ascertain the possibility of causing an allergic condition by the inoculation of lysates and suspensions of dead cultures of the parasite. The experiments were performed on the rhesus monkey (*Macaca mulatta*), since this animal presents, when infected, an immunologic picture similar to that of human patients suffering from trypanosomiasis.

Two monkeys received five preparatory intravenous injections of the antigen at three day intervals. It is important to emphasize the great tolerance of the rhesus monkey for high doses of the antigen. Although the sensitization of the animals was performed by intravenous injections no violent reactions occurred. Twelve days after the last preparatory injection the animals received the shock injection. One monkey was killed eight days after the shock injection, and the second thirty days after the injection. The second monkey received also three more doses after the shock injection, for a better observation of the evolution of the lesions caused by the shock. The lesions observed were of two different types: in the pleura, hyperergic lesions with inflammatory phenomena and development of granulomas; in the heart muscle, a myocarditis reproducing the exact picture found in human American trypanosomiasis.

To exclude the possibility of a toxic action eventually induced by the antigen, two more monkeys were injected. The first received 5 mg. of a desiccated mass of parasites directly into the heart muscle, and, on the same day, 15 mg. of the same material intravenously. The second rhesus received 312 mg. of humid parasites and 42 mg. of dried parasite mass in five injections given at 5 day intervals. No lesions were found in the pleura or in the heart muscle.

Muniz and Azevedo conclude that the killed parasitic bodies behave in the organism like a heterogenous protein with a high sensitizing power and that the lesions described occur as a consequence of the particular conditions of the sensitization. The heart muscle is more sensitive than all other organs and may be considered as a true "shock organ." The complete similarity of the histopathologic picture presented by the rhesus heart muscle in these experiments and the myocarditis observed in human cases of American trypanosomiasis modify the present concept of the pathogenic role of T. cruzi. The theory of an allergic condition in the pathogenesis of such a myocarditis, as suggested in 1929 by Magarinos Torres, finds here its experimental confirmation.

Correspondence

STATE PLANNING CONFERENCE FOR CHILDREN AND YOUTH

To the Editor:--I recently attended the State Planning Conference for Children and Youth in Washington, D. C. (March 30-April 1, 1948). The conference was called by the National Commission on Children and Youth in order to work out a program of action on the state and community level prior to the White House Conference on Children and Youth for 1950. The conference strongly advised the formation of State Committees for Children and Youth in those states not already having such committees, and that these state committees spearhead the formation of community committees. The theme of the 1950 White House Conference is to be "The Child in His Community." In previous White House conferences, decisions were made on the national level at the time of the conference. It is hoped that a well developed program will be under way in every state and community before the 1950 White House conference convenes.

While there were a number of representatives from state health departments, as far as I have been able to determine from the list of delegates, I was the only official delegate from any state medical society. The conference specifically recommended that each state chairman of the American Academy of Pediatrics be named on the State Committee for Children and Youth. It was recognized that these men would be in a better position to interpret the results of the recent Academy of Pediatrics Study of Child Health Services on a state level. It was also felt that state and county medical societies should be represented on these committees. Interestingly enough, these recommendations came from persons outside the medical profession.

The whole tone of the conference indicated that the layman and members of allied professions were most interested in seeking the leadership and advice of the members of the medical profession. Another healthful sign was the emphasis placed on local planning. While the conference was held under the auspices of the Children's Bureau, the government agencies remained much in the background.

In the months ahead members of the medical profession will be asked to serve on State and Local Committees for Children and Youth. It is an opportunity and a challenge which we cannot afford to overlook.

Carl G. Ashley, M.D., Portland, Ore.

NEUROPSYCHIATRY

To the Editor: The term neuropsychiatry has recently come into vogue, especially among the military. This term is unfortunate, since this word - though listed in Webster - is a bastard and a misnomer. Similar words in common usage, such as neurosurgery, neurophysiology and neuroanatomy, naturally lead to the assumption that "neuro" in neuropsychiatry stands for "heurologic." But this is not the case. There is no such thing as neurologic psychiatry. Neither can "neuro" stand for nerve or neuron - as in neuromuscular. "Neuro" is apparently supposed to be an abbreviation of "neurology." If so the term neuropsychiatry is awkward because the endings of the two words are not the same. One rightly abbreviates otology, rhinology and laryngology to otorhinolaryngology, since in this case all endings are the same. If neuropsychiatry is intended to mean an abbreviation of neurology and psychiatry, both of these two words should be used. Each of these disciplines is so large that each deserves to be called by its own full name. One does not say "gyneco-obstetrics," but gynecology and obstetrics. One does not say "ophthalmosurgery" when one means ophthalmology and surgery. A laudable effort to do away with the term "neuropsychiatry" was made at the meeting of the Section on Neuropsychiatry of the California State Medical Association in April 1948. A resolution was adopted to suggest to the council that the name of the section be changed from neuropsychiatry to neurology and psychiatry. A further innovation worthy of imitation has been made in this section under the able chairmanship of Dr. Robert B. Aird of San Francisco. In 1948 the section of neuropsychiatry had two separate sessions, held on separate days: one a psychiatric session, the other a neurology session. This is a better arrangement by far than a program of intermingled papers on neurologic and psychiatric subjects. The interests of neurologists and psychiatrists are drifting too far apart to make a constant mixed program appealing to both. The ideal solution for medical societies, of course, would be the establishment of a separate section on neurology and neurosurgery on one side, and a section on psychiatry on the other. But, for the time being, this idea must remain only the pious wish of some neurologists and neurosurgeons.

ROBERT BARTENBURG, M.D., San Francisco.

AUGMENTATION OF MERCURIAL DIURESIS BY RECUMBENCY

To the Editor:--In connection with the résumé on diuretics by Dr. De Graff (THE JOURNAL, April 17, p. 1025) attention may be called to a simple and useful expedient to enhance the diuretic effect of mercurial compounds, namely, that the patient rest in the recumbent position for eight to twelve hours following administration of the drug.

Newer physiologic investigations are providing clearer insight into the mechanism of congestive heart failure and a better rationale for therapeutic procedures whose value has long been recognized. The beneficent effect of bed rest in cardiac decompensation is due not only to decreasing the work of the heart but in important measure as well to an improvement in the renal circulation. The studies of Warren and Stead (*Arch. Int. Med.* 73: 138, 1944) and others have shown a striking decrease in renal blood flow and glomerular filtration in cardiac failure, with the consequent retention of sodium, a prime factor in the development of edema. The erect position and exercise similarly cause renal vasoconstriction decreasing renal blood flow and glomerular filtration with a fall in diuresis; and particularly is this so in subjects with cardiac failure (Brun, C.; Knudsen, E. O. E., and Raaschou, F.: *Acta med. Scandinav.* 122:315, 1945; Merrill, A., and Cargill, W.H.: *J. Clin. Investigation* 27:272, 1948). The diuretic action of mercury, depending as it does on paralysis of tubular reabsorption of sodium, requires that adequate amounts of sodium and fluid be present in the glomerular filtrate, i.e., an ample renal blood flow and glomerular filtrate. In persons with severe congestive failure who are unresponsive to mercurial diuretics, an increase in renal blood flow brought about by intravenous administration of aminophylline restores the full diuretic effect of mercurials (Weston, R.E., and Escher, D.J.W. in Proceedings Annual Meeting Americal Society for Clinical Investigation, May 3, 1948). The diuretic effect of digitalis in congestive

failure likewise is attributable to an increase in cardiac output and renal blood flow. Measures which increase renal blood flow such as bed rest, the xanthines and digitalis genuinely potentiate the diuretic effect of mercurial compounds.

It is customary to administer mercurial diuretics in the morning so that the patient's sleep is not disturbed due to the necessity for frequent voiding. Ambulant patients treated in the office or clinic should be advised to remain in bed on the day they receive a mercurial injection, so that their diuresis is augmented by the increase in renal blood flow and glomerular filtration resulting from recumbency. In subjects on daily or near daily maintenance dosage of mercurial tablets it is preferable that these be taken at bedtime, since in such circumstances of continued mercurial administration diuresis is seldom sufficiently severe to cause much interference with sleep. An additional advantage is served if mercurial tablets are taken at bedtime, for the nocturnal diuresis helps to minimize the increase in blood volume which occurs when edematous subjects assume the recumbent position and reabsorb into the circulation fluid filtered during the day into the extravascular tissues of the lower extremities. It is this increase in blood volume which is responsible for nocturnal dyspnea. Administration of mercurial tablets on retiring, alone or together with a 0.5 Gm. aminophylline suppository, is effective in decreasing nocturnal dyspnea and in aiding the subject with cardiac decompensation to maintain a normal renal excretion of salt and water.

RICHARD GUBNER, M.D., Brooklyn.

Bureau of Investigation

COURT CALLS KAADTS DISGRACE TO PROFESSION

Sentenced For Violation Of Pure Foods Laws

On April 14, 1948, the Federal District Court jury at Fort Wayne, Ind., found the brothers Charles F. Kaadt and Peter S. Kaadt, doing business as the Kaadt Diabetic Clinic at South Whitley, Ind., and Robert Benson, their superintendent, guilty of violation of the Federal Food, Drug and Cosmetic Act. The defendants had, the jury found, caused to be introduced into interstate commerce a drug misbranded by collateral literature. The drug was vinegar and saltpeter (potassium nitrate). The collateral literature created an impression in the mind of the reader that such drug was a specific for diabetes.

On May 4, 1948, twenty days later, the court reconvened to hear arguments on the motion for a new trial by defense attorneys and to pass sentence. For the brothers Kaadt the court assessed the maximum penalty provided in the statute, namely, one year in jail and a fine of $1,000 for each of the seven counts. It was provided that as to counts 1, 2 and 3 of the indictment each defendant would serve the years consecutively, but counts 5, 6 and 7 were to be served concurrently with count 4, on which sentence was suspended. In addition, the brothers were to be placed on probation for an unstated period, to begin at the end of the serving of the sentence. Assessed equally against each of these defendants were costs which totaled approximately $4,300. Defendant Robert Benson received a suspended sentence of one year. He was fined $50 on each of the seven counts, or a total of $350. He was placed on probation for a period of two years. Peter Kaadt was given ninety days within which to begin serving his sentence. He was brought into the courtroom on a stretcher, because of a heart attack. Charles Kaadt was given ten days within which to begin serving his sentence. Both were denied bond pending appeal.

In sentencing the defendants District Judge Patrick T. Stone said:

> It has taken years of effort on the part of the United States Attorney and the Food and Drug Department to bring you to the bar of justice to answer for your crimes. The proof submitted to the jury as to your guilt was overwhelming. For many years you have been engaged, on a wide scale, in a sordid, an evil and a vicious enterprise, without the slightest regard or consideration for the patients that consulted you seeking relief from diabetes. They were innocent and hopeful, but so gullible. They poured out to you their savings, hoping and believing that you would cure them of their ailment. At all times that you operated your institute, you knew there was no cure for diabetes, that the only recognized treatment for this disease was insulin and a sugar-free diet. Yet, notwithstanding that knowledge, you, in your avarice and greed for wealth, wrongfully advised these trustful patients, and as a result they suffered permanent damage and injury, and perhaps some went to an early grave. You have brought disrepute to your profession, disgrace and dishonor to you and your family. Defendant Charles Kaadt has been operating this health-destroying institute for about ten years. The wheels of justice grind slowly but surely. If you defendants were younger, I would not hesitate to impose the maximum sentences of imprisonment. I shall give to you what you withheld from your patients - some consideration for your condition of health. You were cold, cruel, vicious and heartless in your quest for wealth.

The trial, which lasted for seven days, contained much of the dramatic in the parade of injured witnesses or their survivors and in the testimony of expert medical witnesses. The highlight, however, was the cross examination of Dr. Peter S. Kaadt, who was forced to admit that an insulin deficiency exists in diabetes; that vinegar and potassium nitrate would not produce insulin in the body or bring a patient out of a coma; that he did not know how to make a blood sugar or a dextrose tolerance test, nor could he undertake the determination of a blood level of potassium; nor did he know what the renal threshold is, or what constitutes renal glycosuria. Although on direct examination he had described himself as an expert in diabetes, he had to admit that he took the patients' word for their ailments, that he made no physical examinations and that employees of the Kaadt Diabetic Clinic had prepared the patients' histories. Further, no prescriptions or records of medication were kept.

Dr. Kaadt had testified on direct examination that vinegar had therapeutic value in diabetes, but he admitted to previous testimony before a board of medical examiners that it was a vehicle only. His direct testimony on several other important items was similarly impeached.

The ferric chloride test, "given" the patient with the $30 "treatment," which included some digestive tablets and emodin-bearing pills, was shown to be a test for acidosis and therefore useless as a test for sugar in the urine. That patients should be so misled was forcefully brought to the jury's attention.

Charles F. Kaadt, the prime mover of the scheme, did not take the stand in his defense, nor had he appealed the action of the Indiana Board in revoking his license to practice medicine in Indiana in 1947 for gross immorality in his practice.

The court had permitted the reading into the record part of the proceedings before the Board of Medical Registration and Examination wherein Peter Kaadt's license to practice medicine was revoked for gross immorality in the practice of medicine. Further deliberation by the Court, however, resulted in the request that the jury disregard the recitation. Reference, of course, was to the suc-

ceasful action of the Indiana State Board of Medical Registration and Examination which only recently had been upheld by the State Supreme Court.

On his direct examination, Dr. Peter Kaadt in attempting to show that he was only helping his brother thereby permitted the government to introduce a series of letters on the letterhead of the clinic showing his name. These letters revealed, incidentally, that the quantity of vinegar being purchased monthly amounted to eighteen 50 gallon barrels. The prosecuting attorney's summation recalled testimony that the patients were usually kept in the Clinic for three days at $10 a day and that the medicine was sold for $30 a gallon. The added ingredients, principally potassium nitrate, brought the volume to approximately 1,200 gallons of medicine a month. Thus they were able to demonstrate to the jury an approximate monthly gross income of $60,000.

Expert witnesses for the government were Dr. Elliott P. Joslin, emeritus clinical professor of medicine at Harvard University, Dr. Henry T. Ricketts of the University of Chicago, Dr. John Marvel of the University of Indiana, Dr. Joseph Barach of the University of Pittsburgh and past president of the American Diabetes Association, Dr. Hollo N. Harger, professor and head of the Department of Pharmacology and Toxicology of the University of Indiana and state toxicologist, and Dr. William M. LeFevre, internist of Muskegon, Mich.

The story of insulin therapy with diet and of what such has done for the life expectancy of the diabetic person, particularly in the younger age groups, was brought forcibly and dramatically to the attention of the jury. Dr. Joslin recalled having starved children to enable them to live a bit longer in the hope that something would be discovered that would be a control or a cure for the disease.

In striking contrast was the medical testimony for the defense, led by H. Ward Quartel, an osteopath from Dayton, Ohio. He testified that he was getting good results on a dozen patients in the use of the Kaadt vinegar and saltpeter. Cross examination brought out, however, that his testimony before the Indiana State Board of Medical Registration and Examination on behalf of the Drs. Kaadt was given at about the same time that he obtained the formula from them. That was six months earlier, and he had been using the Kaadt method for the same length of time.

Quartel was followed by two doctors of medicine. Elmer N. Shockley of Bassetts, Va., house physician in an industrial plant, stated he had 1 diabetic patient on whom the Kaadt treatment had been used. It was brought out on cross examination that he had gone to South Whitley to the Kaadt Diabetic Clinic for treatment of his own diabetes, which was, he stated, improved by the vinegar and saltpeter. He also admitted, on cross examination, conversations with a former employee of the Kaadt Diabetic Clinic with a view to opening a similar institution in the East. Such, however, was not done.

Dr. George L. Thompson of Owensboro, Ky., testified that he brought his wife, a sufferer from diabetes, to the clinic. She did not appear as a witness. Cross examination, however, revealed that Dr. Thompson does treat his own diabetic patients with insulin.

Both sides were limited to the introduction of testimony on six items of fact. Six witnesses appeared on behalf of the government, of whom 3 were younger persons with diabetes, 2 were survivors of deceased diabetic patients and the sixth was an amputee. Testifying for the defense were 6 persons who claimed that they were diabetic and had received benefit from the use of the Kaadt treatment. It so happened that 2 of these had recently been examined by other physicians who came to Fort Wayne to testify in rebuttal for the government. Each of the " satisfied " customers of the Drs. Kaadt had 4 plus sugar.

Perhaps the most damaging witness to the brothers Kaadt was a boy aged 15 who had gone to the Clinic because his mother had heard of the " cure. She had other children at home and could not remain with him at the clinic. This lad took notes of a lecture delivered by Dr. Charles Kaadt (as was clinic custom) and testified from these notes that Dr. Kaadt had told his listeners, among other things, that " whisky is good for diabetes"; " boiled sugar is safe"; " the less insulin the better," and "if you have a diet, throw it away."

The Kaadt Diabetic Clinic has been in operation for a good many years. Dr. Charles F. Kaadt started out in Fort Wayne, Ind., during the twenties. He had been a surgeon for the Wabash Railroad. The Bureau of Investigation reported on the matter in THE JOURNAL of Aug. 15, 1931. The report at that time told of the attempt on the part of the Bureau to learn the details of the treatment, which was then being sold by mail, a quart bottle costing $5. The medicine at that time was described as a material which indicated the presence of potassium nitrate in fairly large amounts, dissolved in a brown, murky liquid having the odor of vinegar. Over the years, the only change seems to have been the increase to gallon lots with digestive and laxative pills as the components of the home treatment also being carried away by the victims. On cross examination Peter Kaadt complained that medical science quit when it discovered insulin.

In the past, adversity, in the form of action denying the use of the mails, which earlier had disrupted active interstate distribution of this nostrum, only served to solidify the business of Dr. Charles Kaadt. When it became so large that he could no longer handle it alone, his brother joined with him.

So for the institution has had the benefit of the investigative action of the Better Business Bureau of Indianapolis, the *Indianapolis Star*, the Indiana State Board of Medical Registration and Examination, the Post Office Department and now the Food and Drug Administration and the Department of Justice. Withal it has taken considerable effort and enormous expense to place the present obstacles in the path of the prosecution of this business. During the trial the institution was being operated under the guidance of Dr. Archie Jones, of Fort Wayne and other Indiana points. Newspapers, during the trial carried a report that he was to be cited by the Indiana State Board of Medical Registration and Examination to show cause why his license to practice medicine should not be revoked. More recent reports do indicate, however, that the Kaadt Diabetic Clinic has finally closed its doors.

The government was ably represented by United States Attorney Alex M. Campbell and his assistants, James S. Keating and Gilmore S. Haynie. The defendants had Frank E. Corbett and Lloyd Hartzler of Fort Wayne as counsel. Congratulations are certainly in order to the office of the United States Attorney for skilful handling of the case in such a manner that a favorable verdict was reached by the jury within a relatively short period of time. The investigation of the Food and Drug Administration as the preliminary to the court action bore such fruit as to indicate its efficiency. It is the hope of the Bureau that these events may serve as discouragement to others who may seek to capitalize on uninformed fear of the insulin needle.

Medical Motion Pictures

FILM REVIEW

Daily Battle. 16 and 35 mm., black and white, sound, 800 feet (one reel), showing time twenty minutes. Produced in 1947 by RKO Pathe, Inc., through the cooperation of McCook Memorial Hospital, Hartford, Conn. Procurable on loan or purchase from the National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

This film is a vivid portrayal of the services provided by the March of Dimes, through national and local chapters of the National Foundation for Infantile Paralysis. It was designed to show how the funds are used in the fight against poliomyelitis and the constant vigil necessary to meet the handling of these cases. The film can be recommended for showing to hospital personnel, physical therapists and those persons interested in rehabilitation problems.

The Feeling of Rejection: Its Development and Growth. 16 mm., black and white, sound, 800 feet (1 reel), showing time twenty minutes. Prepared in 1947 with the technical advice of the Medical staff of the Allen Memorial Institute of Psychiatry, McGill University and the Royal Victoria Hospital, Montreal, for the Mental Health Division of the Department of National Health and Welfare, Ottawa. Produced and procurable on rental or purchase from the National Film Board of Canada, 400 West Madison Street, Chicago 6, and 620 Fifth Avenue, New York 20.

This film portrays the case of Margaret, who at the age of 22 complains to a psychiatrist that she is shy, moody and indecisive to the point of self frustration. Placed on a gynecologic table in lieu of an analytic couch, Margaret recounts the story of her life and thus furnishes the script for a series of flashbacks in familiar Hollywood styles. Margaret's mother is accused of inculcating fears of normal initiative and exploratory play in Margaret's childhood, after which Margaret is shown experiencing rivalry with a younger sibling, feeling rejected by her parents frustrated in substitutive attachments to an idealized school friend and so on. To an experienced analyst these retrospective fantasies can mean little more than literalized "screen memories," yet they are presented in the film as the cause rather than the accompaniment of defensive personality traits such as exaggerated meticulousness, masochistic discipline and resentful isolation.

From a technical point of view the film has a number of other defects: the musical interpolations are distracting and amateurish, and the commentary is occasionally so tedious and pontifical that the net effects are painful rather than poignant.

Psychologically, the film oversimplifies the nature of "feeling of rejection" and fails to clarify the complex sexual inhibitions, repressed hostilities and other unconscious conflicts that underly Margaret's obsessive-compulsive neurosis. Certainly, the implication that such deep seated character deviations can be corrected in a few therapeutic interviews is seriously misleading.

On the favorable side, this is a commendable first attempt to present some of the modern concepts of dynamic psychiatry to lay or ancillary professional groups. Despite the explanatory pamphlet that accompanies the film, however, a competent psychologist or psychiatrist should be present to clarify and amplify its message and so prevent misunderstanding of its content.

The following 16 mm., black and white sound motion pictures are part of a series of five films produced in 1947 by the McGraw-Hill Book Company for correlation with the Textbook of Healthful Living, prepared by Harold S. Diehl, M.D., dean of the medical sciences, University of Minnesota, Minneapolis. Procurable on purchase from McGraw-Hill Book Company, Inc., 330 West Forty-second Street, New York 18, or procurable on rental from Y.M.C.A. Motion Picture Bureau, 19 South La Salle Street, Chicago 3.

Emotional Health. 725 feet (one reel), showing time twenty minutes.

The continuity of this motion picture is characterized by excellent writing, competent acting and good medical sense. A youth consults a general practitioner for "heart trouble" and receives the usual diagnostic examination. He is told that he is in normal physical condition but that his cardiac symptoms may be due to functional disturbances arising from emotional stresses. The physician's explanations, clear and concise in themselves, are illustrated by sequences of action and cartoon animation which, though somewhat oversimplified, would be illuminating to a lay audience. The youth is then advised to consult a psychiatrist, and his objections to the referral are dispelled by further reassurances that could serve as a model for many a practitioner. Excerpts from several of the patient's subsequent interviews with the psychiatrist--for once portrayed as a perceptive and rational human being--are then recorded, and the patient's anxieties are traced to conflictful familial, sexual and social attitudes. Throughout this section of the film typical episodes that may have led to the formation of disturbing unconscious conflicts are recalled in vivid flashbacks relevant to the patient's childhood experiences. Although the interviews are of necessity somewhat telescoped, the course of the therapy is presented in logical and convincing sequence and with a validity that stems from authoritative supervision.

This film can be highly recommended not only for the teaching of medical undergraduates but for presentation to lay groups interested in some of the principles of psychosomatic medicine and brief psychotherapy.

Body Care and Grooming. 600 feet (one reel), showing time sixteen minutes.

The importance of personal cleanliness, good grooming and proper attention to clothing is well depicted in this film in a way that would be acceptable to the average college student. The structure and activity of the skin are shown in diagrammatic animation. The motivation for cleanliness and care of the body is extremely effective, and, though it is particularly aimed at students of college age, there is no apparent reason why it would not be equally useful for high school groups. It could be used in mixed as well as in segragrated groups.

A silent follow-up film strip, consisting of scenes selected from the corresponding motion picture over which questions are superimposed, accompanies each motion picture. Photography is excellent and the animation is well done.

The following was omitted from the motion picture review entitled "HUMAN REPRODUCTION" which appeared in THE JOURNAL, A.M.A., May, 1948, p. 323:

The following 16 mm., black and white sound motion picture is a part of a series of five films produced in 1947 by the McGraw-Hill Book Company for correlation with the Textbook of Healthful Living, prepared by Harold S. Diehl, M.D., Dean of the Medical Sciences, University of Minnesota, Minneapolis. Procurable on purchase from McGraw-Hill Book Company, Inc., 330 West Forty-second Street, New York 18, or procurable on rental from Y.M.C.A. Motion Picture Bureau, 19 South La Salle Street, Chicago 3.

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194

An Introduction To Extracellular Fluid. 16 mm., black and white, sound, 800 feet (one reel), showing time twenty-five minutes. Prepared in 1945 by James L. Gamble, M.D., professor of pediatrics, Harvard University Medical School, Boston. Produced by and procurable on loan from Mead Johnson & Company, Evansville 21, Ind.

The author presents a lecture based on a highly technical subject to which he has devoted much time and effort over a period of years. The chemistry and physiology of extracellular fluid have been his chief medical interest, together with the application of basic principles to the clinical aspects of fluid balance in health and disease. This picture will be of interest to those who studied under the author and to those interested in fluid balance. However, to those who are looking for a teaching film containing the modern devices, this picture will be a disappointment because it shows the self-effacing scientist, rather ill at ease before the sound camera, presenting his subject in lecture form with the aid of two charts. It might have been preferable to portray the author in his laboratory, at his desk or in the ward in lieu of standing before an unseen group of students.

Coming Medical Meetings

American Medical Association, Chicago, June 21-25. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Aero Medical Association, Royal York Hotel, Toronto, Canada, June 15-19. Dr. Thomas H. Sutherland, 214 S. State St., Marion, Ohio, Secretary.

American Academy for Cerebral Palsy, Baltimore, May 30-31. Dr. Meyer A. Perlstein, 4743 N. Drake Ave., Chicago 25, Secretary.

American Academy of Tuberculosis Physicians, Chicago, June 19. Dr. Oscar S. Levin, P. O. Box 7011, Denver 5,

American Association for the Surgery of Trauma, Drake Hotel, Chicago, June 17-20. Dr. Charles G. Johnston, 1512 St. Antoine St., Detroit 26, Secretary.

American Association for Thoracic Surgery, Quebec, Canada, May 31-June 2. Dr. Brian Blades, 1335 H St. N.W., Washington 5, D.C., Secretary.

American Association of the History of Medicine, Penn Sheraton Hotel, Philadelphia, May 25-27. Dr. Howard Dittrich, 2020 E. 93rd St., Cleveland 6, Secretary.

American Blood Irradiation Society, Stevens Hotel, Chicago, June 19-20. Dr. G. J. P. Barger, 1125 Buchanan St. N.W., Washington, D.C., Secretary.

American College of Chest Physicians, Congress Hotel, Chicago, June 17-20. Dr. Benjamin L. Brock, 500 N. Dearborn St., Chicago 10, Secretary.

American College of Radiology, Sheraton Hotel, Chicago, June 20. Mr. Mac F. Cahal, 20 N. Wacker Drive, Chicago 6, Executive Secretary.

American Diabetes Association, Chicago, June 17-20. Dr. George E. Anderson, 429 Clinton Avenue, Brooklyn 5, Secretary.

American Electroencephalographic Society, Claridge Hotel, Atlantic City, June 12-13. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 15, Secretary.

American Heart Association, Stevens Hotel, Chicago, June 19-19. Dr. Harry E. Ungerleider, 50 W. 50th St., New York, Secretary.

American Medical Women's Association, Blackstone Hotel, Chicago, June 19-20. Dr. Helen T. Batterman, 125 Wm. Taft Road, Cincinnati 19, Corresponding Secretary.

American Neurological Association, Claridge Hotel, Atlantic City, June 14-15. Dr. H. Houston Merritt, 100 E. Gun Hill Road, New York 67, Secretary.

American Orthopedic Association, Quebec, Canada, June 3-5. Dr. C. Leslie Mitchell, Henry Ford Hospital, Detroit 2, Secretary.

American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery, Academy of Medicine Bldg., New York, June 10. Dr. Norman N. Smith, 291 Whitney Ave., New Haven 11, Conn., Secretary.

International Poliomyelitis Conference, Waldorf-Astoria Hotel, New York, July 12-17. Mr. Stanley E. Henwood, Room 571, Waldorf-Astoria Hotel, New York 22, Executive Secretary.

Maine Medical Association, Poland Spring House, Poland Spring, June 20. Dr. Frederick R. Carter, 142 High St., Portland 3, Secretary.

Massachusetts Medical Society, Hotel Statler, Boston, May 25-27. Dr. H. Quinby Gallupe, 8 Fenway, Boston 15, Secretary.

Medical Library Association, Warwick Hotel, Philadelphia, May 28-30. Miss M. Edna Poole, 288 Bloor St. W., Toronto 5, Canada, Secretary.

Minnesota State Medical Association, Minneapolis, June 7-9. Dr. B. B. Sonster, 490 Lowry Medical Arts Bldg., St. Paul 2, Secretary.

Montana, Medical Association of, Billings, June 17-19. Dr. H. T. Caraway, 115 N. 28th St., Billings, Secretary.

National Gastroenterological Association, Hotel Pennsylvania, New York, June 7-10. Dr. G. Randolph Manning, 1819 Broadway, New York 23, Secretary.

National Tuberculosis Association, Hotel Pennsylvania, New York, June 14-18. Dr. H. Stuart Willis, 1790 Broadway, New York 19, Secretary.

New Hampshire Medical Society, Newcastle, June 2-3. Dr. Carleton R. Metcalf, 5 S. State St., Concord, Secretary.

New Mexico Medical Society, Las Vegas, June 3-5. Dr. H.L. Jamuary, 221 W. Central Ave., Albuquerque, Secretary.

North Dakota State Medical Association, Jamestown, May 23-25. Dr. O. A. Sedlak, 702 First Avenue S., Fargo, Secretary.

Society for Investigative Dermatology, Hotel Sherman, Chicago, June 20. Dr. Samuel M. Peck, 140 E. 54th St., New York 22, Secretary.

Society for Vascular Surgery, Hotel Stevens, Chicago, June 20. Dr. J. Ross Veal, 1020 Connecticut Ave., Washington 6, D. C.

South Dakota State Medical Association, Sioux Falls, May 30-June 1. Dr. Roland G. Moyer, 224 S. Main St., Aberdeen, Secretary.

Southern Society of Clinical Surgeons, Chicago, May 26-28. Dr. William P. Nicolson Jr., 478 Peachtree St. N. E., Atlanta, Ga., Secretary.

American Pediatric Society, Quebec, Canada, May 24-26. Dr. Henry G. Poucher, 1019 W. Polk St., Chicago 12, Secretary.

American Physiotherapy Association, La Salle Hotel, Chicago, May 23-28. Miss Mildred Elson, 1790 Broadway, New York 19, Executive Secretary.

American Proctologic Society, Chicago, June 18-21. Dr. Vernon G. Jourish, 1612 Tremont Place, Denver 2, Secretary.

American Radium Society, Hotel Stevens, Chicago, June 20. Dr. Hugh F. Hare, 605 Commonwealth Ave., Boston 15, Secretary.

American Rheumatism Association, Hotel Stevens, Chicago, June 19-20. Dr. Charles Ragan, 620 W. 168th St., New York 32, Secretary.

American Surgical Association, Chateau Frontenac, Quebec, Canada, May 27-29. Dr. Warfield M. Firor, Johns Hopkins Hospital, Baltimore 5, Secretary.

American Therapeutic Society, Chicago, June 20. Dr. Oscar B. Hunter, 1835 I St. N.W., Washington 6, D. C., Secretary.

American Venereal Disease Association, Chicago, June 20. Dr. William L. Fleming, 750 Harrison Ave., Boston, Secretary.

Association for the Study of Internal Secretions, Palmer House, Chicago, June 18-19. Dr. Henry H. Turner, 1200 N. Walker St., Oklahoma City 3, Secretary.

Idaho State Medical Association, Sun Valley, July 5-8. Dr. Wallace Bond, 144 E. Fourth Ave., Twin Falls, Secretary.

Interamerican Cardiological Congress, Michael Reese Hospital, Chicago, June 13-17. Dr. Richard Langendorf, Michael Reese Hospital, 29th and Ellis, Chicago 16, Secretary.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Boards in Specialties were published in THE JOURNAL, April 17, page 1064.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Examination. Montgomery, June 22-24, 1948. Sec., Dr. D.G. Gill, 519 Dexter Ave., Montgomery 4.

ARKANSAS:* Examination. Little Rock, June 3-4. Sec., Medical Board of the Arkansas Medical Society, Dr. L.J. Kominsky, Texarkana. Eclectic: Little Rock, June 3. Sec., Dr. C.H. Young, 1415 Main St., Little Rock.

CALIFORNIA: Oral. San Francisco, June 5-6; Los Angeles, Aug. 7-8. Written Examination. San Francisco, June 7-10. Los Angeles, Aug. 9-12. Oral and Clinical Examination for Foreign Graduates. San Francisco, June 6. Sec., Dr. Frederick N. Scatena, 1020 N. Street, Sacramento 14.

COLORADO:* Examination. Denver, June 21-23. Final date for filing application is June 5. Sec., Dr. J.B. Davis, 831 Republic Bldg., Denver.

CONNECTICUT:* Examination. Hartford, July 6-7. Sec., Dr. Creighton Barker, 258 Church St., New Haven.

DELAWARE: Examination. Dover, July 13. Endorsement. Dover, July 22. Sec., Dr. J.S. McDaniel, 229 S. State St., Dover.

FLORIDA:* Examination. Jacksonville, June 29-30. Sec., Dr. Harold D. Van Schaick, 6675 Windsor Lane, La Gorce Island, Miami Beach 41.

GEORGIA: Examination. Atlanta, June 8-9. Endorsement, June 10. Sec., Mr. R.C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Examination. Honolulu, July 12-15. Sec., Dr. S.E. Doolittle, 881 S. Hotel St., Honolulu.

IDAHO: Boise, July 13-15. Sec., Bureau of Occupational Licenses, Miss Estella S. Mulliner, 355 State House, Boise.

ILLINOIS: Chicago, June 29-July 1. Supt., Dept. of Registration and Education, Mr. Fred W. Ruegg, Springfield.

INDIANA: Examination. Indianapolis, June 15-17, 1948. Sec., Board of Medical Registration and Examination, Dr. Paul B. Tindall, 416 K. of P. Bldg., Indianapolis.

KANSAS: Kansas City, June 9-10. Sec., Board of Medical Registration & Examination, Dr. J.F. Hassig, 905 N. 7th Ste., Kansas City.

KENTUCKY: Examination. Louisville, June 16-18. Sec., Dr. P.E. Blackerby, 620 S. 3rd St., Louisville.

LOUISIANA: New Orleans, June 3-5. Sec.-Treas., Dr. Roy B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MAINE: Augusta, July 6-7, Sec., Dr. A.P. Leighton, 192 State Street, Portland.

MARYLAND: Medical Examination. Baltimore, June 15-18. Sec.-Treas., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. Homeopathic Examination. Baltimore, June 15-16. Sec., Dr. J.A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Examination. Boston, July 13-16. Sec., Board of Registration in Medicine, Dr. H.Q. Gallupe, 413-E. State House, Boston.

MICHIGAN:* Examination. Parlor A, Olds Hotel, Lansing, June 9-11. Sec., Board of Registration in Medicine, Dr. J.E. McIntyre, 100 W. Allegan St., Lansing.

MISSISSIPPI: Jackson, June 28-29, 1948. Asst. Sec., State Board of Health, Dr. R.N. Whitfield, Jackson.

MONTANA: Helena, Oct. 4-6. Sec., Dr. O.G. Klein, First Nat'l Bank Bldg., Helena.

NEBRASKA:* Examination. Omaha, June 7-9. Dir., Mr. Oscar E. Humble, Room 1009 State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: Concord, Sept. 9. Sec., Board of Registration in Medicine, Dr. J.S. Wheeler, Room 107, State House, Concord.

NEW JERSEY: Examination. Trenton, June 15-17. Sec., Dr. E.S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO:* Santa Fe, Oct. 11-12. Sec., Dr. V. E. Borchtold, 141 Palace Ave., Santa Fe.

NEW YORK: Examination. Various Centers, June 28-July 1. Sec., Dr. J.L. Lochner Jr., State Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, July 6-9. Sec., Dr. G.M. Williamson, 4½ S. 3rd St., Grand Forks.

OHIO: Examination. Columbus, June 21-24. Sec., Dr. H.M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* Oklahoma City, June 2-3. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* Examination. July and Jan. Endorsement. July and Aug. Sec., Miss L.M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Examination. Philadelphia & Pittsburgh, July. Act. Sec., Bureau of Professional Licensing, Mrs. M.G. Steiner, 351 Education Bldg., Harrisburg.

RHODE ISLAND:* Examination. Providence, July 1-2. Chief, Div. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Written Examination. Columbia, June 21-23. Endorsement, July 5. Sec., Dr. N.B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Pierre, July 20-21. Sec., Dr. Gilbert Cottam, Capitol Bldg., Pierre.

TENNESSEE:* Examination. Memphis & Nashville, June 9-10. Sec., Dr. H.W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Waco, June 16-18. Sec., Dr. H.F. Connally, 1305 Amicable Bldg., Waco.

UTAH: Examination. Salt Lake City, June, 1948. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

VERMONT: Examination. Burlington, June 25-26. Sec., Dr. F.J. Lawliss, Richford.

VIRGINIA: Examination. Richmond, June 18-19. Endorsement, Richmond, June 17. Sec., Dr. K.D. Graves, 306 Medical Arts Bldg., Roanoke.

WEST VIRGINIA: Charleston, July 5-7. Coun., Public Health Council, Dr. N.H. Dyer, State Capitol Bldg., Charleston.

WISCONSIN:* Milwaukee, June 29-July 1. Sec., Dr. C.A. Dawson, Tremont Bldg., River Falls.

WYOMING: Examination. Cheyenne, June 7. Sec., Dr. G.M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Examination. Tucson, June 15. Sec., Mr. Francis A. Roy, Univ. of Arizona, Tucson.

COLORADO: Examination. Denver, June 2-3. Sec., Dr. E. B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: Examination. June 12., Exec. Asst., State Board of Healing Arts, Mr. W.G. Reynolds, 110 Whitney Ave., New Haven 10.

IOWA: Des Moines, July 13, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MINNESOTA: Examination. Minneapolis, June 1-2. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis.

OREGON: Examination. Portland, June 19. Final date for filing application is June 2. Sec., Basic Science Examining Committee, Dr. C.D. Byrne, Univ. of Oregon, Eugene.

SOUTH DAKOTA: Examination. Vermillion, June 4-5. Sec., Dr. G.H. Evans, 310 E. 15th St., Yankton.

TENNESSEE: Examination. Memphis, July 5-6. Sec., Dr. O.W. Hyman, 874 Union Ave., Memphis.

WISCONSIN: Examination. Madison, Sept. 25. Final date for filing application is Sept. 18. Sec., Prof. W.H. Barber, Scott & Watson Sts., Hipon.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Narcotics: Physicism's Right to Possess Narcotics Unlawfully Obtained.—The defendant was convicted of unlawfully possessing a narcotic drug and from such conviction appealed to the court of criminal appeals of Texas.

A patient of the defendant physician testified that his wife was given a prescription calling for fifteen tablets of 1/16 grain (4 mg.) "Dilaudid Hcl" (dihydromorphinone hydrochloride) which was taken to a pharmacist and properly filled. The patient then returned to the physician's office and gave him the box which the pharmacist had given her. He took it into his private office. A little while later he delivered to the patient a box of pills which were subsequently analyzed as "novocaine" hydrochloride and not "Dilaudid" hydrochloride. "Novocaine" hydrochloride is not a derivative of opium, but "Dilaudid" hydrochloride is. It was the contention of the state that the defendant physician came into possession of the narcotic by taking the same from the filled prescription and substituting another drug therefor--in other words, that the defendant acquired the narcotic by theft, subterfuge or fraud and that therefore his possession of it was unlawful. The defendant contended that he had the right to possess narcotics.

Section 2 of the uniform narcotic act provides that "It shall be unlawful for any person to... possess...any narcotic drug." Section 2 A provides that "It shall not be unlawful to...possess... any narcotic drug where same is authorized under the terms of this Act." These two sections, 2 and 2 A, said the court, are a part of the same act and are of equal dignity. They must therefore be construed together. When so construed, they must mean that if the act authorizes possession of a narcotic, such possession is lawful; otherwise, it is not. It becomes material, then, the court continued, to determine wherein the act authorizes possession of a narcotic and if the defendant has discharged the burden resting upon him to bring himself within those provisions. A physician--that is, one authorized by law to practice medicine--in this state may in good faith, in the course of his professional practice only, prescribe, administer and dispense narcotic drugs. The term dispense as there used, in addition to its ordinary meaning, includes "distribute, leave with, give away, dispose of or deliver." The terms prescribe and administer--not being specially defined--are used in their ordinary meaning, as commonly known and understood. So, then, a physician may in the course of his professional practice prescribe, administer, dispense, distribute, leave with, give away or deliver a narcotic. The right to do these things carries with it the right to possess, because possession is first necessary and without it such rights could not be fully exercised. The term possession, as here used, means the actual care, control and management of the narcotic.

If we understand the state's position, said the court of criminal appeals, it is that since there are facts sufficient to show that the defendant came into the possession of the narcotic by unlawful means, he could not thereafter be in the lawful possession thereof. To accept this theory would require, by judicial construction, writing into the act an additional limitation not found therein--which would be that unless and until a physician came into possession of a narcotic by lawful means, he could not make use of the same in any manner. The act authorized the physician to make unlimited use of the narcotic in the particulars mentioned. We would not be authorized, said the court, by judicial construction, to place a limitation on that right not found in the act. In the light of what has been said, there appears no escape from the conclusion that, under the rights expressly conferred under the act, it is not unlawful for the physician duly licensed by the laws of this state to have in his possession, or possess, narcotic drugs. Since the defendant was a duly licensed practitioner of medicine in this state, his conviction for possessing a narcotic drug is accordingly reversed.—*De Vine v. State, 206 S. W. (2d) 247 (Texas, 1947).*

Blood Grouping Tests: Admissibility in Evidence over Objection of Self Incrimination.—The defendant was found guilty of murder in the first degree and appealed to the Court of Appeals of Maryland.

At the time of the defendant's arrest, he was in a hospital under treatment for iodine poisoning and after being placed in jail he was treated by the county medical officer. The following day another physician visited him, at the request of the state's attorney, for the purpose of getting a sample of his blood. The physician testified that the captain of detectives, who accompanied him on the visit, asked the defendant if he would mind if he took his blood. The defendant held out his arm, the physician took some of his blood and turned the specimen over to the officer. The physician also testified that he listened to the defendant's heart and took his pulse, but did not tell him why he wanted the blood other than that the state's attorney requested it. The captain of detectives corroborated this testimony and said that, in addition, the physician asked if the medicine the county physician had given him the previous night had worked. He too stated that when he asked the defendant if he had any objection to their getting a sample of his blood, the defendant said no and held up his arm to the physician. The defendant was not informed of the purpose for which they wanted the blood specimen. The defendant testified that the physician asked him if he knew that the iodine he had taken might affect his eyes or his kidneys and said that he would like to take a blood test and a urine specimen. The defendant said he thought they were doing it for his health.

On appeal the defendant contended that the admission of testimony about his blood, taken from his body by a subterfuge, was a violation of his constitutional immunity from giving evidence against himself. We are unable to see where there is any constitutional question involved in this case, the Court of Appeals concluded. There is no substantial difference between obtaining a specimen of blood from an accused and obtaining his fingerprints or physical property, the possession of which by him is a pertinent question at issue in a felony against him. Whatever may be the rule in other jurisdictions we have long since adopted the rule that the admission of evidence thus obtained is not a violation of the Maryland Declaration of Rights, and we so hold in this case. Accordingly the judgment of conviction was affirmed.—*Davis v. State 57 A. (2d) 289 (Md., 1948).*

Extravagant Claims and Promotional Literature as Misbranding.--The defendant was charged with a violation of the federal food, drug and cosmetic act for introducing misbranded drugs into interstate commerce. From a judgment of conviction, the defendant appealed to the circuit court of appeals, seventh circuit.

Section 301 of the food and drug act prohibits the introduction or delivery for introduction into interstate commerce of any drug that is misbranded; section 502 provides that a drug shall be deemed to be misbranded if its labeling is false or misleading in any particular, and section 201 (a) defines the term "labeling" to include all labels and other written, printed or graphic matter accompanying such article.

The defendant was a self-styled authority on nutrition and vitamins. Operating under various trade names, he had been producing and marketing his products since January 1941, largely through "health food" stores. The products appear to be, for the most part, compounded of various vitamins, minerals and herbs. No charge of falsehood was made as to the principal labels printed on the packages in which each product was contained. The misbranding charged was contained in a number of printed pamphlets and circulars, and one display placard. The mode of distribution of this literature differed. In some cases it was contained in the carton in which the articles were shipped. More often, it was separately shipped to the same consignees, and in at least one case a period of a year and a half intervened between the shipment of the product and the literature, respectively.

In order to support a misbranding charge, said the court, it is not necessary that the matter alleged to accompany the product be shipped in the same container or even that it be shipped simultaneously. The defendant contended that the literature here involved was not only not shipped in the same carton with the products in all cases, but neither was it intended by him that product and literature should be placed together by the dealer to whom they were sent. His theory was that the literature was intended for advertising, not labeling. All the printed matter, he said, was intended either to be mailed out or to be sold, as indicated by the fact that with the exception of the one display placard, each piece either contained a price mark or a mailing permit with space for address. This showed he contended, that product and literature were not to be distributed together, hence could not be said to accompany each other.

First, said the court, labeling and advertising are not mutually exclusive and the same matter may serve both purposes. Second, the placing of the mailing permit or the price tag on the literature cannot insulate the defendant from liability for introducing the drugs and their related descriptive matter into interstate commerce together by consignment to the same consignee for distribution by him.

The test, the court continued, is not of physical contiguity but of textual relationship. Viewed thus, the products and literature here involved were interdependent because the former lacked the labeling necessary to inform the purchasing public of their uses and purposes. The labels printed on the immediate containers did not indicate the purposes for which the articles were to be used. The literature was intended and essential to explain the alleged uses of the products. It constituted a supplement to the label physically attached to the container of the product. One of the health food dealers in whose store the "kordel" products were sold admitted that if he were buying one of the products he would have to go to "reliable sources" to know to what use to put the product. Presumably, said the court, those reliable sources were the booklets displayed in racks close by the counter where the drugs were dispensed or lying on the counter where they were available to the public and could be picked up and examined. Some also were wrapped with merchandise or handed to customers. Because the literature was shipped by the defendant or at his order to the same consignees as the products, was related to those products, and was intended for distribution in relation to them, it did accompany the products into interstate commerce within the definition of the act.

With respect to the misrepresentations contained in the accompanying literature, said the circuit court of appeals, we think there can be no serious question. The two booklets, "Nutrition Guide" and "What You Can Do About Relieving the Agonies of Arthritis," were written by defendant, who in the latter is described as "America's leading vitamin and diet expert." "Health Today, Spring 1945," is edited by the same "famous nutrition and vitamin authority." While all purport to be scientific publications of general interest apart from the articles produced and marketed by the defendant, all are replete with references to the "kordel" products and their uses to prevent, ameliorate or cure a vast and diverse variety of ailments, and each conveniently closes with a price list of the various "kordel" products recommended for use therein. All are concerned primarily with promoting the sale of the various products by explaining the need for each, along with extravagant claims as to the usefulness of each. A study of the three pamphlets reveals that the products therein described are recommended for relieving stomach agonies, general weakness, anemia, premature old age, high blood pressure, liver troubles, failing eyesight and sore feet; for maintaining blood energy, muscular activity, sound teeth and gums, healthy skin, hair and eyes, normal functioning of the pituitary and thyroid glands, stomach, intestines, colon, liver and kidneys, and for preventing arthritis and stiff joints, excess weight, catarrh, nervous breakdown, sterility and paralysis. Thus the scheme devised by the defendant for the distribution of his products and related literature contemplates an elaborate system of self diagnosis and medication. The government introduced the evidence of many eminent men in the medical profession to prove the dangerously misleading character of the literature in that the drugs were useless to combat the conditions they were represented to relieve, while delay in correct diagnosis and treatment for those conditions might render treatment useless. All the experts were agreed that, although the claims were absurd and fantastic, they were dangerous in that they tended to lull persons into a false sense of security in reliance on the drugs when they might need professional diagnosis and treatment for conditions which might respond to treatment if correctly diagnosed early enough, but which might become much more serious if not taken care of early. Since the literature, which we have already held accompanied the products, embodies such misleading representations, the court of appeal concluded, it constitutes misbranding within the meaning of the act. Accordingly the conviction of the defendant was affirmed.--*United States v. Kordel, 164 F. (2d) 913 (1948).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 10 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

17:213-256 (Jan.) 1948

Heart Disease in Alabama. O. Welch and C. Porter.—p. 213.
Resection of Midthoracic Esophagus for Carcinoma. W. C. Simpson.—p. 221.
Calibration and Use of Photoelectric Colorimeter. H. H. Crookshank.—p. 226.
Caudal Analgesia. W. E. Lloyd.—p. 233.
Chronic Mastoiditis. E. R. Hodine.—p. 237.

17:257-292 (Feb.) 1948

Acute Abdomen. C. N. Carraway.—p. 257.
Penicillin, Streptomycin and Tyrothricin in Dermatology. P. G. Roque.—p. 260.
Fracture of Edentulous Mandible: Open Reduction and Fixation with Tantalum Wire. G. V. Matthews.—p. 273.

American J. Digestive Diseases, Fort Wayne, Ind.

15:1-40 (Jan.) 1948

Acute Pancreatitis: Evaluation of Classification, Symptomatology, Diagnosis and Therapy. H. L. Popper. p. 1.
Contribution to Diagnosis of Acute Pancreatic Necrosis. H. F. Herfort.—p. 5.
Jaundice and Hepatitis: Laboratory Review. S. H. Rabson.—p. 7.
Indications and Contraindications for Gastroscopy. H. Barovsky.—p. 10.
Gastritis and Amebiasis: Gastroscopic Study. T. C. Afendulis.—p. 13.
Appliance for Preventing Leakage of Gastrostomy and Enterostomy. A. Strelinger.—p. 14.
Allergy as Factor in Headaches. J. A. Turabull.—p. 16.
Carcinoma of Colon Secondary to Chronic Ulcerative Colitis. T. H. Johnson and T. G. Orr.—p. 21.
*Importance of Occult Blood in Stool. W. D. Paul and H. E. Hamilton.—p. 23.

Occult Blood in the Stool.—Paul and Hamilton believe that digital examination of the rectum and the test of a fecal specimen for occult blood should be a routine part of physical examination. Earlier recognition of a disease process in the gastrointestinal tract will be made if this simple and expedient procedure is carried out. A technic employed at the University of Iowa hospitals is as follows: Following the digital examination, the gloved finger is placed over the top of a 3/4 inch (1.91 cm.) test tube containing 5 cc. of water. The tube is shaken so that the adhering stool specimen is washed from the end of the gloved finger, and a drop of this solution is placed on a small piece of filter paper. An orthotolidine tablet is placed on this moistened filter paper and 2 drops of water are permitted to flow over the tablet and down on the filter paper. If occult blood is present, the filter paper about the orthotolidine tablet will turn a blue color of varying intensity within two minutes. Even though there is no visible fecal material adhering to the gloved finger the material obtained will frequently be sufficient to give a positive reaction if the preceding stool specimen contained occult blood.

American J. Obstetrics and Gynecology, St. Louis

55:1-188 (Jan.) 1948

Metallic Sutures and Early American Gynecology. H. P. Bucher.—p. 1.
Human Conceptus During First Two Weeks of Gestation. J. Hoch and A. D. Hertig.—p. 6.
Studies of Human Corpus Luteum. Corpus Luteum-Endometrial Relationships in Functional Uterine Bleeding. J. I. Brewer and H. O. Jones.—p. 18.
Atypical Endometrial Hyperplasia Simulating Adenocarcinoma. E. Novak and F. Rutledge.—p. 46.
*Use of Multiple Sources of Radium Within Uterus in Treatment of Endometrial Cancer. A. N. Arneson, V. W. Stanbro and J. F. Nolan.—p. 64.
High Lymphadenectomy and Sympathectomy in Carcinoma of Vulva. E. M. Robertson.—p. 79.
Detailed Anatomy of Paraurethral Ducts in Adult Human Female. J. W. Huffman.—p. 86.
*Culdoscopy a Useful Gynecologic Procedure. R. W. TeLinde and F. Rutledge.—p. 102.
Resections of Vulva to Systemic Diseases. J. Parks and Shirley Martin.—p. 117.
Clinical and Histopathologic Study of Lesions of Cervix Uteri During Pregnancy. C. F. Fluhmann.—p. 133.
Cervical Dystocia with Special Reference to Fibrous Nature of Cervix. O. H. Schwarz and R. B. Woolf.—p. 151.
Expectant Management of Placenta Previa. T. J. Williams.—p. 169.

Radium in Uterus.—Arneson and his associates say that about 1938 the method of radium treatment of uterine cancer was changed in two hospitals in St. Louis. Previously intrauterine treatment had been given by means of tandems containing from two to three tubes in linear arrangement. That applicator did not always meet the standard requirement of active length extending from the level of the external os to the top of the fundus. The first modification, which employed gauze strips to hold multiple tubes in position, did not prove satisfactory. Many technical difficulties were eliminated by a special instrument developed in 1940. By means of an introducer the number of tubes placed within the uterus was increased considerably. Brass capsules of a standard external diameter were obtained for radium sources. Length of capsules varied according to length of the radium tubes, but the strength per centimeter active length was on the order of 5 or 6 mg. of radium. From ten to twelve such capsules can be packed into a uterine cavity of normal size. Capsules of greater external diameter are used in the cervical canal to maintain patency adequate for removal of the intrauterine radium. Stronger sources are used in the cervical capsules. The authors review observations on 93 patients with endometrial cancer treated between 1936 and 1941. Of the entire group, 45 per cent were considered inoperable. The absolute five year survival rate for the 43 patients treated by radiation alone is 27 per cent. For the 32 patients receiving preoperative roentgen and radium therapy followed by hysterectomy the five year result is 68 per cent. Surgery alone was used in 18 patients, of whom 84 per cent remained well for the same period. Explanation of the unusually good results from hysterectomy alone is made on the basis of favorable clinical material. Among patients treated by radiation alone the use of intrauterine tandems resulted in survival of only 22 per cent, but 32

per cent of those irridiated with multiple capsules are well at the end of the five year period. For treatment by radiation and hysterectomy the use of intrauterine tandems resulted in survival of 54 per cent, but the value for multiple capsules of radium is 79 per cent.

Culdoscopy.—TeLinde and Rutledge report their experience with culdoscopy in 56 cases. The patient is placed in the knee-chest posture. The procedure can be carried out under local or general anesthesia. The uterus, tubes, ovaries, broad ligaments, uterosacral ligaments, infundibulopelvic ligaments, rectal wall, sigmoid, small intestines and often the cecum, appendix and even the ureters can be visualized. The culdoscope may be moved from side to side and rotated as necessary. Culdoscopy is indicated particularly to gain more information in cases in which the history and/or pelvic examination suggest tubal pregnancy. Of the 56 cases of culdoscopy reported here, 37 were for this purpose. Ectopic gestation is more often overlooked and more often diagnosed when not present than any other serious pelvic disorder. Salpingitis was found to be the condition simulating tubal gestation in 18 of the 37 cases. The differential diagnosis between salpingitis and endometriosis may at times offer considerable difficulty. The culdoscopic pictures in both conditions are quite characteristic, and the differentiation is easily made unless the cul-de-sac is obliterated by adhesions. In postmenopausal bleeding culdoscopy may detect a nonpalpable ovarian or tubal neoplasm. In certain endocrine disturbances, such as functional bleeding, functional amenorrhea, ovarian dwarfism and ovarian agenesis, exact knowledge of the anatomic and to some degree the physiologic condition of the ovaries can be obtained only by culdoscopy or exploratory laparotomy. The chief contraindication to culdoscopy is the presence of a fixed mass in the cul-de-sac. The authors regard culdoscopy as a valuable adjunct to gynecologic procedures.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

59:1-156 (Jan.) 1948 Partial Index

*Physiobiology and General Management of Chronic Ulceration Occurring After Irradiation. H. B. Hunt and D. H. Breit.—p. 9.
Master Facial Cast for Rigid Portal Delimitation in Roentgen Therapy of Cancer About Face. S. G. Castiglione.—p. 19.
Herniation of Cerebral Ventricles. C. R. Perryman and E. P. Pendergrass.—p. 27.
Diagnostic Significance of Change in Position of Metallic Foreign Bodies in Brain Abscess. E. H. Wood, Jr.—p. 52.
Some Observations on Diffuse Pulmonary Lesions. H. Felson and G. B. Heublein.—p. 59.
Basal Onset of Reinfection Tuberculosis. H. H. Cherry.—p. 82.
Crater in Uncomplicated Duodenal Ulcer: Its Significance in Diagnosis and Treatment. F. E. Templeton.—p. 87.
*Postbulbar Ulcer of Duodenum. H. P. Ball, A. L. Segal and R. Goldes.—p. 90.
Bernard Schmidt and His Reflector Camera: Astronomical Contribution to Radiology. P. C. Hodges.—p. 122.

Ulceration After Irradiation.—Influences which may contribute to ulceration following irradiation include, according to Hunt and Breit, systemic disorders such as hypoproteinemia, ascorbic acid (vitamin C) deficiency, allergy, anemia, arteriosclerosis, uncontrolled diabetes and syphilis; poor blood supply; infection of devitalized tissue; foreign body action of devitalized bone, cartilage or fascia; trauma—whether actinic, thermal, mechanical or chemical; inadequate regeneration of tissue due to nutritional disorders; residual or recurrent neoplasm. The occurrence of necrosis following irradiation is to be reduced by promotion of general health, provision of proper nutrition, preservation of blood supply, control of infection, protection against trauma, treatment of lesions while small, and elimination of cancer by the first course of therapy as far as possible. Experimental studies on acute radiodermatitis in rabbits showed onset to be delayed and severity reduced by avoidance of greasy applications, although the reaction was not aggravated by water or dry powder. Clinical observations suggest that the vesicular phase is benefited by sterile blend wet dressings and exposure to the air. Infection can be reduced by prompt closure of the skin and by bacteriostatic and antibiotic drugs. There are various ways to eliminate necrotizing tissues. The use of radon ointment is most effective in promoting regeneration of epithelium.

Postbulbar Ulcer of Duodenum.—According to Ball and his associates, ulcer craters in the duodenum are not commonly found distal to the bulb, but since there is hemorrhage in many of these cases, often of the massive type, it is important that a careful search be made for ulcer craters in the examination of the upper portion of the gastrointestinal tract. Ulcer of the duodenum located distal to the bulb displays a smooth, rounded indentation of the wall at the level of the crater with an eccentric narrowing in all cases examined. Enlarged, distorted mucosal folds, irritability of the bulb and hypermotility are associated observations. The ulcer crater is not always seen. The use of exaggerated oblique projections with the patient in the horizontal position or with the head lowered below the horizontal plane has been found to be helpful in disclosing the lesions of postbulbar ulcer. The incidence of postbulbar ulcer is difficult to evaluate. In cases of hemorrhage from the gastrointestinal tract, particularly in those cases associated with back pain and symptoms of peptic ulcer, the possibility of postbulbar ulcer should be seriously considered.

Annals of Internal Medicine, Lancaster, Pa.

28:1-228 (Jan.) 1948

Pathogenesis of Lupus Erythematosus and Allied Conditions. P. Klemperer. -p. 1.
Cardiac Lesions of Acute Disseminated Lupus Erythematosus. Eleanor H. Humphreys. -p. 12.
Physical Examination: Helps and Hindrances. J.J. Waring. -p. 15.
*Urine Volume and Total Renal Sodium Excretion During Water Diuresis. A.J. Crutchfield Jr. and J.E. Wood Jr. -p. 28.
*Incidence of Heart Disease in 2,000 Consecutive Autopsies. W.B. Wartman and H.K. Hellerstein. -p. 41.
Rheumatism and Arthritis: Review of American and English Literature of Recent Years (Ninth Rheumatism Review). P.S. Hench and others. -p. 66.

Urine Volume and Total Renal Sodium Excretion.—Crutchfield and Wood say that the advisability of drastically reducing sodium intake in the edema of congestive heart failure is generally accepted. Recommendations concerning the optimal water intake during such sodium restriction, have ranged from the older view that fluids should be drastically restricted to the opposite extreme, that fluids should be forced even to 5 or 10 liters daily. The authors decided to investigate how fluid intake might be adjusted to assure in the average patient the greatest possible excretion of sodium per day. Approximately one hundred observations on water diuresis and sodium excre-

tion have been made on 50 patients. Water diuresis was produced by oral administration of 1,000 cc. of tap water within fifteen minutes. It was found that in a patient who already has adequate urine volume, the exhibition of water diuresis does not increase total renal sodium excretion. To the contrary, in such a patient water diuresis usually decreases total renal sodium excretion. It is further suggested that the optimal urine volume for the patient with congestive heart failure, when related to water diuresis alone, falls between 2 and 3 liters daily. The efficiency of osmotic diuretics is impaired when combined with water diuresis. Xanthines and mercurophylline injection disproportionately increase urinary volume and total renal sodium excretion, favoring the latter. This suggests that the primary renal action of these substances may be depression of tubular reabsorption of sodium.

Incidence of Heart Disease.—Wartman and Hellerstein present a statistical study of the incidence of heart disease in 2,000 consecutive necropsies. The term heart disease is used in an anatomic sense and includes all organic lesions of the pericardium and heart, but it does not necessarily mean clinically evident disease. Nearly two thirds of the necropsies involved males. The age curve of the series was similar to that of deaths from all causes in the United States Registration Area for 1940. Forty-nine and two-tenths per cent of the patients had some cardiac lesion, although not all were sufficiently important to have contributed to death. Nineteen per cent died directly of heart failure. The cardiac lesions were divided into rheumatic heart disease, hypertensive heart disease, coronary artery disease and a miscellaneous group. Thirteen and six-tenths per cent of the total group had hypertensive heart disease. The age, sex and color distribution of 120 patients with rheumatic heart disease was as follows: the mitral valve was involved in every case, the aortic in 85, the tricuspid in 53 and the pulmonic in 15. Forty-nine patients with rheumatic carditis lived to be 45 years old or more. There were 16 cases of endocarditis lenta among the 120 cases of rheumatic heart disease. The coronary arteries were significantly diseased in 51 per cent of the 984 patients with heart lesions, or 25 per cent of the total series. Eighty-four per cent of patients with coronary thrombosis also had myocardial infarcts; 16 per cent died without myocardial infarcts, many of them suddenly. The factors concerned in sudden death following coronary obstruction were severe generalized coronary arteriosclerosis and multiple occlusions with occlusion of the predominant artery. The incidence of myocardial infarcts in the total necropsy series was 8.2 per cent. The left ventricle was the most frequent site of an infarct. The commonest complications of myocardial infarction were mural thrombi, fibrinous pericarditis, subsequent myocardial infarcts, aneuryam formation and cardiac rupture. Peripheral thromboembolism occurred in 45 per cent of cases of myocardial infarcts and were a main or contributory cause of death in 43 of 160 cases.

Archives of Otolaryngology, Chicago

47:1-112 (Jan.) 1948

Question of Prothrombinopenic Hemorrhage from Post-Tonsillectomy Use of Chewing Gum Containing Acetylsalicylic Acid. G. S. Livingston and E. R. Neary.—p. 1.

Plastic Repair of Obstructing Nasal Septum. S. Fomon, J. G. Gilbert, A. G. Silver and V. R. Syracuse.—p. 7.

*Chemical Meningitis Following Use of Tyrothricin: Clinical and Experimental Study. F. J. Otenasek and D. Fairman.—p. 21.

Nonvibratory Tinnitus. Factors Underlying Subaudible and Audible Irritations. E. P. Fowler.—p. 29.

*Nasal Hemorrhage. Studies of Ascorbic Acid, Prothrombin and Vitamin K. H. Neivert, Hecha Engelberg and L. A. Pirk.—p. 37.

Congenital Laryngeal Web: Its Eradication. D. L. Poe and P. S. Seager.—p. 46.

Morphologic Deformities of Lower Lateral Cartilages. J. Daley.—p. 49.

Paranasal Sinuses. S. Salinger.—p. 72.

Chemical Meningitis Following Use of Tyrothricin.—Otenasek and Fairman have not found reports of ill effects in human beings from clinical use of tyrothricin. They report 2 patients seen at the Johns Hopkins Hospital exhibiting disastrous effects from this drug. Morbid effects in both patients were seen immediately after a frontal sinus had been irrigated with tyrothricin. There were severe headache, delirium, high fever and, in a very few hours, clinical and laboratory signs of meningitis. In both, the acute inflammatory process lasted less than a week, with apparent clinical cure but with delayed production of hydrocephalus as a consequence of adhesive arachnoiditis. The first patient had a stormy convalescence and left the hospital with no perception of light in the right eye and disturbance of visual acuity in the left. There also was some unsteadiness. The second patient died. Necropsy revealed hydrocephalus and chronic meningitis with thickening and round cell infiltration of the leptomeninges. The clinical experience with these 2 patients prompted experiments on animals. Of 35 dogs in whom 1 cc. of a 1:1,000 suspension of tyrothricin was injected into the cisterna magna, 18 died either immediately or within a few hours. Those with a survival period of a few hours showed massive swelling of the medulla oblongata at the site of injection, with almost complete obliteration of the foramen of Magendie in some cases. Animals surviving longer periods were killed at different intervals. The final picture revealed gross and microscopic thickening of the leptomeninges, with or without hydrocephalus. The authors stress that even extremely small amounts of tyrothricin in the cerebrospinal fluid may produce disastrous effects. When an opening of the dura mater is known to exist after a radical sinusotomy, irrigations with this agent should be scrupulously avoided. Routine and indiscriminate tyrothricin irrigation of infected cavities close to the subarachnoid space is to be avoided.

Nasal Hemorrhage.—Neivert and his associates studied 104 consecutive patients presenting themselves with nosebleed at the Presbyterian Hospital, New York. Ascorbic acid level and prothrombin time were normal in only 11 of these patients. The plasma ascorbic acid level was subnormal in 68 patients, of whom 35 also showed prothrombinopenia. There were 25 patients whose plasma ascorbic acid concentration was normal but whose prothrombin activity was subnormal. The nosebleed in 57 patients was traceable to one of the generally recognized local or systemic causes, but in 47 patients it was not. Vitamin therapy was instituted in 62 of the 93 patients found to be deficient in ascorbic acid and/or prothrombin. The clinical response could be determined in only 36 patients. Of these, 27 were improved. The extremely high incidence of ascorbic acid and prothrombin deficiency in cases of epistaxis and the gratifying clinical results attending the administration of ascorbic acid and/or a vitamin-K-like substance in some of these cases suggest that vitamins C and K have a definite place in the management of nasal hemorrhage.

Blood, New York

3: 1-128 (Jan.) 1948

Treatment of Pernicious Anemia by Special Diet. G. R. Minot and W. P. Murphy.—p. 8.
Pernicious Anemia from Addison to Folic Acid. R. L. Haden.—p. 22.
Twenty Years of Liver Therapy. W. P. Murphy.—p. 32.
*Pernicious Anemia, Nutritional Macrocytic Anemia, and Tropical Sprue. Lucy Wills.—p. 36.
*Relation of Therapy in Pernicious Anemia to Changes in Nervous System, Early and Late Results in Series of Cases Observed for Periods of not Less Than Ten Years, and Early Results of Treatment with Folic Acid. F. H. Bethell and C. C. Sturgis.—p. 57.
*Development and Progression of Subacute Combined Degeneration of Spinal Cord in Patients with Pernicious Anemia Treated with Synthetic Pteroylglutamic (Folic) Acid. J. F. Ross, H. Belding and B. L. Pespel.—p. 68.
Pernicious Anemia Caused by Diphyllobothrium Latum, in Light of Recent Investigations. R. Von Bonsdorff.—p. 91.
Study of Myelogram (Bone Marrow Puncture) in Pernicious Anemia and Problem of Megaloblast. J. Wallerad.—p. 103.
*Refractory Megaloblastic Anemia. L. S. P. Davidson.—p. 107.
Further Observations on Specificity of Folic Acid Molecule. T. D. Spies, G. G. Lopez, R. E. Stone and others.—p. 121.

Macrocytic Anemias.—Wills limits her discussion to the three principal types of macrocytic anemia: pernicious anemia, nutritional macrocytic anemia and tropical sprue. The interrelationship of these three entities is reviewed on the basis of reports in the literature and of unpublished work. The author considers these three clinical conditions as distinct entities possessing a common characteristic in the presence of a panhemopoietic dystrophy characterized by a megaloblastic erythropoiesis and corresponding changes in the myeloid cells and platelets. This panhemopoietic dystrophy possibly results from the breakdown of an intracellular enzyme system, but the deficiencies causing the breakdown differ; in pernicious anemia the liver principle is apparently at fault, in endemic nutritional macrocytic anemia another unidentified factor is missing and in sprue either or both may be at fault. Folic acid is active therapeutically in all three diseases, but in all it fails to restore completely normal blood levels. Pernicious anemia is probably due to a genetic defect which produces atrophy of the gastric mucosa. As a consequence of this interference with gastric function there is failure in the formation or absorption of the liver factor and possibly of another neurotropic factor, which failure results in the development of a macrocytic megaloblastic anemia and the characteristic changes in the nervous system. Indefinite replacement therapy is necessary, as the changes in the gastric mucosa are irreversible. Endemic nutritional macrocytic anemia is a food deficiency in a factor other than the liver principle, possibly a coenzyme present in or associated with good biologic protein and the vitamin B_2 complex. A hemolytic type of the disease occurs in areas of high malarial incidence. After successful treatment the disease does not relapse if the diet is satisfactory. Pregnant women are particularly liable to development of the disease. Tropical sprue is due to a functional disorder of the intestine, possibly primarily a failure in phosphorylation of fatty acids, glycerol and dextrose. Diarrhea and macrocytic anemia are present. The macrocytic anemia may be due to a failure in absorption of one or more essential hemopoietic factors or to a lack of Castle's intrinsic factor. A high protein diet and liver extract are most important in the treatment.

Therapy and Nervous System in Pernicious Anemia.—Bethell and Sturgis analyzed the clinical course, particularly the neurologic changes, in 70 patients with pernicious anemia, who were observed for periods of not less than ten years. Most of the patients, whether treated with oral preparations of stomach or liver, or with parenteral crude or refined liver extracts, showed significant improvement of their neurologic manifestations. The period of improvement was limited, essentially, to the first year of therapy. Thirty-six patients were maintained in complete hematologic remission. Fifteen of the patients did not adhere to an optimal therapeutic regimen, and their blood values were frequently abnormal, although definite relapses did not occur. In the former group there was no progression of neural lesions. In the latter such adverse changes as did occur were transient and reversible on resumption of adequate therapy. Nineteen patients had clinical and hematologic relapses after their initial response to intensive therapy. The end results in this group were not so favorable, but nevertheless serious progression of spinal cord involvement was seldom observed. The observations do not justify the conclusion that irregular or suboptimal therapy is without serious risk. The early results of treatment with synthetic folic acid, as observed in 15 patients, indicate that both the hematologic and the neurologic response to this form of therapy are much less predictable than is the case with stomach or liver preparations. It is suggested that disturbance of folic acid metabolism is not the sole cause of either the hematologic or the neurologic manifestations of pernicious anemia but that inability to utilize folic acid effectively may play a part in the development of both myeloid and neural abnormalities.

Spinal Cord Degeneration and Folic Acid.—Ross and his associates substituted synthetic folic acid (pteroylglutamic acid) for liver extract in treatment of 22 patients with pernicious anemia. The patients received this treatment for from eight to seventeen months. Satisfactory blood levels were maintained in all cases receiving daily oral doses of 1.25 to 15 mg. Severe hematologic relapse occurred within six months in a case treated with monthly injections of 30 mg. of the preparation. Synthetic folic acid in oral doses of 15 mg. daily induced satisfactory hematopoietic responses in 3 patients with pernicious anemia in severe relapse, but only slight hematopoietic response was obtained in a fourth patient with mild pernicious anemia but severe subacute combined degeneration of the spinal cord. Ten patients manifested a significant improvement in blood values for a few months after substitution of folic acid for liver extract. With one exception these subsided after six or more months to pre-folic acid levels comparable with those previously maintained with liver extract alone. These observations suggest that a combination of orally administered folic acid and parenterally injected liver extract may maintain a better hematologic status than either substance alone. A previously untreated patient with severe subacute combined degeneration of the spinal cord failed to show improvement in neural disease during twenty-eight days of folic acid therapy. Eleven patients manifested, or showed progression of, subacute combined degeneration of the spinal cord during folic acid treatment. Neurologic disease developed in most of these patients when the peripheral blood was normal. The institution of liver extract therapy in addition to folic acid in 5 patients in whom there developed subacute combined degeneration during folic acid maintenance therapy failed to prevent progression of the disease in 4 cases and only

partially arrested the disease in the fifth, in which improvement occurred more rapidly when folic acid was discontinued. Subacute combined degeneration occurred with greater frequency in patients on large daily doses of folic acid than it did in patients with small or intermittent doses. This suggests the possibility that folic acid in large daily doses may actually precipitate or aggravate neurologic disease.

Refractory Megaloblastic Anemia.—Davidson applies the term refractory megaloblastic anemia to cases which failed to respond hematologically and clinically to the parenteral administration of an amount of liver extract which has been proved to produce an optimal response in cases of addisonian pernicious anemia. The preparation employed had been found to be potent in a dose of 2 cc. when administered parenterally in a large number of cases studied during the past ten years. Every patient with refractory megaloblastic anemia received at least twice this dose after admission to hospital. During the past six years 59 patients with megaloblastic anemia partially or completely refractory to potent liver extracts given parenterally have been investigated in Edinburgh. Thirty-four of these cases were associated with pregnancy, the puerperium or the sprue syndrome. No explanation of the cause of the megaloblastic anemia was discovered in the remaining 25 cases. Excellent therapeutic effects were obtained by proteolysed liver or folic acid in the 25 cases of idiopathic refractory megaloblastic anemia. With regard to the mechanisms involved in refractoriness to potent parenteral liver extracts the author suggests that chemical purification of liver extracts for parenteral use may remove some essential factor which is necessary for the restoration of normal blood formation in certain cases of megaloblastic anemia. It is possible that an unknown hematinic principle, in addition to the liberating factor in purified parenteral liver extract and folic acid, is required for the complete restoration of normoblastic blood formation.

Diseases of Nervous System, Chicago

9:1-28 (Jan.) 1948. Partial Index

Management of Speech Disorders in Hospital Clinic. V. G. Peacher and Georgiana H. Peacher. -p. 3.
Maintenance Treatment in Schizophrenia. S. Weiss and Jane N. Creel. -p. 10.
*Clinical Trial of 10820, New Synthetic Analgesic. N. A. Bercel. -p. 15.
Review of Literature on Group Treatment of Psychoses. S. Gifford and J. Mackenzie. -p. 19.
Observations Noted During Course of Group Treatment. J. Fidler Jr. and C. Standish. -p. 24.

Clinical Trial of New Synthetic Analgesic.—Bercel says that the new analgesic drug 6-dimethylamino-4, 4-diphenyl-3-heptanone, known as 10820 or methadon, appears to have a morphine-like effect. Administrations of 2.5 mg. of Methadon raised the pain threshold to the same extent as did 10 mg. morphine sulfate. Bercel summarizes experiences with this new analgesic drug on 25 selected patients, all of whom had severe pain. The drug was given in various doses and in a variety of ways. More or less complete relief from pain was obtained by all but 3 patients. Ten patients complained of side effects. In 5 administration of the drug had to be discontinued because of undesirable reactions due to sensitivity. Skin tests are advisable. After daily administration of 5 to 60 mg. of the drug for periods varying from two to twelve weeks, the sudden withdrawal produced no physiologic withdrawal phenomena. The drug appeared to be a potent analgesic with an effect similar to morphine and demerol.

Journal of Mount Sinai Hospital, New York

14:891-940 (Jan.-Feb.) 1948

Application of Isotope Technic to Problems of Biology and Medicine. D. Rittenberg.—p. 891.
Intestinal Irrigation in Treatment of Certain Types of Uremia: Preliminary Report. G. D. Oppenheimer and S. Rosenak.—p. 908.
Convulsions Under General Anesthesia. J. Borchan and B. H. Elizenberg.—p. 912.
Aneurysms of Anterior Portion of Circle of Willis Causing Cerebral Hemorrhage. M. Ostow and S. Berman.—p. 918.
Auricular Tachycardia and Auriculo-Ventricular Dissociation Following 1.2 Mg. of Digitoxin in One Dose. J. Stone.—p. 924.
Foreign Body in Second Portion of Duodenum Perforating Pelvis of Right Kidney. M. J. Hackby.—p. 929.
Effusion in Temporomandibular Joint Complicated by Otitis Media. J. G. Druss.—p. 931.
Cecostomy for Prolonged Colonic Ileus. H. E. Leiter and A. S. Lyons.—p. 934.

J. Neuropathology & Exper. Neurology, Baltimore

7:1-122 (Jan.) 1948

Pallial Component in Hepato-Lenticular Degeneration. R. Richter.—p. 1.
*Hemochromatosis of Central Nervous System. Hans A. Neumann.—p. 19.
Studies on Physiology and Therapy of Convulsive Disorders: II. Some Properties of Experimental Convulsions. J. E. P. Toman, E. A. Swinyard, H. Merkin and L. S. Goodman.—p. 35.
Mode of Extension of Contrast Substances Injected into Peripheral Nerves. J. D. French, H. H. Strain and G. E. Jones.—p. 47.
*Myotonia Atrophica: Histopathologic Considerations. G. B. Hassin and B. Kesert.—p. 59.
Bone Formation and Destruction in Hyperostoses Associated with Meningiomas. H. Freedman and F. H. Forster.—p. 69.
Multiple Primary Intracranial Tumors. Meningioma Associated with Glioma: Report of Case. W. S. Alexander.—p. 81.
Human Pyramidal Tract. XVI. Resection of Individual Axons in Selected Cases with Acute Cerebral Lesions. A. H. Lassek.—p. 89.

Hemochromatosis of Central Nervous System.—Neumann says that hemochromatosis, so named by von Recklinghausen, was first isolated by him as a clinical entity in 1889. Since that time more than 300 cases have been reported. Sheldon's study lists the chief criteria for the recognition of the disease as follows: brown pigmentation of the skin, widespread pigmentation of the viscera, muscles and connective tissues, cirrhosis of the liver and pancreas, and diabetes. Pigmentation of the brain is seldom mentioned in case reports, although it has been stated that the choroid plexus is almost uniformly involved. Neumann's case greatly resembled that reported by Lewey and Govons. There was relatively slight involvement of the viscera. The main neurologic signs accompanying the disorder are progressive ataxia and deafness. The cerebrospinal fluid is xanthochromic. Vomiting occurs frequently. The primary pathologic process is believed to have originated in the teloid roof of the fourth ventricle. In Neumann's case the superior surface of the cerebellum was intensely damaged. It is probable that this case and the few similar recorded cases constitute a clinicopathologic entity.

Histopathologic Aspects of Myotonia Atrophica.—Hassin and Kesert present the results of histopathologic studies on 3 patients with myopathies together with brief summaries of the clinical aspects. They stress that in myotonia atrophica there is a disproportion between the pathologic and clinical features. Myotonia atrophica is a definite morbid entity embodying some clinical features of

myotonia congenita, progressive degenerative myopathies and extra muscular dystrophies (cataracts, baldness and other anomalies). The histologic changes are not specific, being similar to those seen in paramyoclonus multiplex and myotonia congenita (Thomsen's disease), but differ from those occurring in exquisitely inflammatory and degenerative diseases of the muscles. Myotonia atrophica is, like myotonia congenita and paramyoclonus multiplex, a metabolic disturbance which is probably responsible for the abnormal muscular activity that ultimately brings on pathologic changes.

Journal of Pediatrics, St. Louis

32:1-112 (Jan.) 1948

*Treatment of Acute Respiratory Infections in Children with Orally Administered, Unbuffered Penicillin Solutions. W. S. Hoffman, J. W. Hofer and H. Gordon. —p. 1.
Glomerular Filtration Rate, Effective Renal Blood Flow and Maximal Tubular Excretory Capacity in Infancy. J. R. West, H. W. Smith and H. Chasis. —p. 10.
New Anomaly of Aorta. Left Aortic Arch with Right Descending Aorta. R. N. Paul. —p. 19.
*Treatment of Pertussis and Pneumonia Complicating Pertussis. Role of Hyperimmune Gamma Globulin and Sulfadiazine. H. Brainerd. —p. 30.
*Restoration of Diptheria Immunity Without Injections (Bousfield's Method). P. Masucci, H. Gold and R. J. DeFalco. —p. 35.
Heart in Normal Infants and Children. Incidence of Precordial Systolic Murmurs and Fluoroscopic and Electrocardiographic Studies. N. Epstein. —p. 39.
Eosinophilic Granuloma of Bone and Hand-Schuller-Christian Disease. Frances M. Love and Gladys J. Foshens. —p. 46.
Petechiae in Children: Incidence, Seasonal Variations and Etiology. E. E. Brown. —p. 55.
Acrodynia: New Treatment with BAL. L. Bivings and G. Lewis. —p. 63.
Adjustment of Parents to Children in Home. S. Berman. —p. 66.

Oral Penicillin for Respiratory Infections.—Hoffman and his co-workers treated 143 infants and children who had acute respiratory infections with a palatable solution of soluble tablets of crystalline potassium penicillin G without buffers. Dosage to be used every three hours for each age group was determined by an evaluation of assays of the plasma penicillin levels obtained after single doses in 209 control infants and children. Those between the ages of 1 and 12 years showed, one hour after the dose, average levels of 0.12 unit per cubic centimeter, and at three hours, 0.03 to 0.05 unit per cubic centimeter. Though dosage had been based on age, therapeutic plasma levels were obtained with doses of approximately 3,000 units per kilogram (or 1,400 units per pound). Infants under 1 year showed much higher levels, well sustained after three hours. High penicillin concentrations were probably produced by the relatively poor renal function of such young infants. In 94 (65.7 per cent) of the patients treated, fever subsided within forty-eight hours and clinical improvement occurred. Fair results were achieved in 26 (18.2 per cent) and poor results in 23 (16.1 per cent). Evaluation on the basis of positive bacterial cultures or high white blood cell counts only slightly increased the percentage of satisfactory results. Yet it was certain that a virus component was present in many cases. Plasma penicillin levels obtained were of the same order as those found in assays. Urticaria occurred in only 1 patient and there was only occasional vomiting. Thus oral administration of penicillin without buffers is to be considered a convenient and satisfactory method of treatment of respiratory infections in children, if adequate doses are used. Failure of response in forty-eight hours is the signal for increased dosage or change to parenteral penicillin.

Pertussis and Pneumonia Complicating Pertussis.—Brainerd treated 26 infants, average age 7.9 months, who had whooping cough complicated by pneumonia and 26 infants, average age 9.4 months, who had uncomplicated pertussis; he gave intramuscular injections of 2.5 cc. of pertussis hyperimmune gamma globulin on each of four successive days with a total dose of 10 cc. All patients with pneumonia were also treated with sulfadiazine. Response to treatment in the first group with pneumonia was considered excellent in 2, good in 9, moderate in 7 and equivocal in 5; 1 patient became worse, although he later recovered. Two patients died. In the second group results of treatment were excellent in 14, good in 4, moderate in 4 and equivocal in 4. No patient became worse or died. It was striking that no patient in this group contracted pneumonia or any other complication of pertussis. Hyperimmune gamma globulin appeared to shorten the course, lessen the severity and reduce the rate of complications. In combination with sulfadiazine it appeared to affect favorably the mortality rate of pertussis complicated by pneumonia. The maximum therapeutic effect of hyperimmune gamma globulin was obtained in patients treated during the first seven days of illness.

Bousfield's Reimmunization Against Diphtheria. Masucci and his co-workers gave a varied dose of hard compressed tablets in which diphtheria toxoid was incorporated to a group of 22 persons who had been immunized previously or had at some time come in contact with diphtheria, and to a second group of 15 Schick-positive persons who had no previous history of immunization or of exposure to the disease. In the first group some were given four tablets for seven days; others received three tablets for seven days and the remainder of the group received two tablets daily for seven days. The second group received four tablets daily for seven days. The tablets were placed under the tongue until they disintegrated completely. Bousfield's observation that diphtheria toxoid antigen can be absorbed effectively by the mucous membranes of the upper portion of the alimentary tract has been confirmed. In general persons who had received previous diphtheria antigen or who had been exposed to the disease showed a definite increase in antitoxin titer. In some the increase was pronounced. This method of immunization was ineffective in those persons who apparently never had a primary stimulus. The amount of antigen absorbed is sufficient to act as a booster dose but is not sufficient to provide an adequate stimulus for primary immunization. There were no local or general reactions. Bousfield's method therefore appears to be the most promising of all the nonparenteral methods of reimmunization thus far proposed. The large dose required (2,100 Lf units) may hinder its practical application.

Minnesota Medicine, St. Paul

31:1-120 (Jan.) 1948

Follow-Up Diagnosis on Patients with X-Ray Lesions with Special Emphasis on Tuberculosis. H. Roesmich. —p. 29.
Evaluation of Anticoagulant Therapy in Deep Venous Thrombosis of Lower Extremities. C. Dennis. —p. 37.
Early Postoperative Ambulation. C. H. Heed. —p. 40.
Hypertension—Medical Treatment. W. D. Coventry. —p. 42.
Hypertension—Surgical Treatment. H. F. Buchstein. —p. 45.
Abdominal Emergencies in General Practice. J. F. Norman. —p. 49.
Bowel Obstruction. Analysis of 148 Cases. A. C. Skjold. —p. 52.

New England Journal of Medicine, Boston

238:73-106 (Jan. 15) 1948

Present-Day Status of Poliomyelitis. W. T. Green.—p. 73.
*Treatment of Polycythemia Vera by Spray Irradiation. W. Richardson and L. L. Robbins.—p. 78.
Ovarian Conservation During Surgery with Reference to Bilateral Dermoids and Endometriosis. A. A. Levi.—p. 83.
Thoracic Tenderness in Pulmonary Infarction. J. Godfrey.—p. 86.
Syphilis. G. M. Crawford.—p. 87.
Carcinoma of Breast: Metastases to Lungs, Liver, Axillary, Mediastinal and Retroperitoneal Lymph Nodes, Ovary and Vertebrae. Chylous Ascites and Hydrothorax.—p. 94.
Malignant Lymphoma, Reticulum-Cell Sarcoma Type, Involving Mediastinal and Other Lymph Nodes, Kidneys, Adrenal Glands, Lungs, Intestine, Stomach, Thyroid Gland and Bones.—p. 97.

Spray Irradiation in Polycythemia Vera.—According to Richardson and Robbins, treatment of polycythemia vera by spray irradiation was instituted at the Massachusetts General Hospital in 1932. Irradiation is given with the intention of covering a field extending from the neck to the knees. This requires a long target-skin distance, which varies from 215 to 250 cm., and can usually be accomplished with a 20 by 20 cm. cone. The area is centered at the level of the crest of the ilium, and anterior and posterior fields are treated on alternate days. The kilovoltage is 200; filtration is obtained with 0.5 mm. of copper and 1 mm. of aluminum, which gives a half layer value of 0.92 mm. of copper. The daily dose varies from 20 to 30 r measured in air, and the total dose in a series of treatment in usually 500 r. A white blood cell count is taken at the end of a week and at shorter intervals as the cells decrease. Treatment is stopped when the count falls below 5,000 to 6,000. Twelve of the 28 patients who have received spray irradiation for polycythemia vera are dead, but 4 died of causes other than the disease or its treatment. Of the 16 living patients, 13 are free of symptoms attributable to polycythemia; 1 has hypertension, 1 is anemic and 1 is still polycythemic and is considered a therapeutic failure. One patient has a refractory anemia, possibly or probably attributable to roentgen therapy. In no patient has there developed leukemia, a leukemic state or myeloid metaplasia. Phlebotomy is contraindicated in polycythemia vera except in the treatment of acute symptoms. Spray irradiation is considered the treatment of choice. The use of radioactive isotopes is discussed briefly.

Pennsylvania Medical Journal, Harrisburg

51: 385-480 (Jan.) 1948

Trends in Modern Psychiatry. N. D. C. Lewis.—p. 405.
Surgical Management of Hypertension. J. W. Shirer.—p. 410.
Program of Commission on Public Health and Preventive Medicine. P. F. Lucchesi.—p. 415.
*Life Expectancy in Cancer of Prostate. R. P. Beatty.—p. 419.
Diagnosis and Treatment of Migraine. Edith E. Nicholls.—p. 423.
Abnormal Uterine Bleeding. E. J. Bateman.—p. 427.
Stem Pessary in Management of Primary Dysmenorrhea. E. A. Schumann and M. L. McCall.—p. 431.
Anesthetic Management of the Aged. C. S. Turville and R. D. Dripps.—p. 434.

Life Expectancy in Cancer of Prostate.—Beatty points out that it is seven years since investigation of the effect of endocrines on prostatic carcinoma was initiated. In this period management of this disease has been completely revolutionized. A life expectancy of one to two years has been lengthened to an average of three years, during most of which time the patient lives in comparative comfort. In this series, which covers a period of about five years, the average life expectancy of the patients who have been followed is 3 years for those still living and 3.4 years for those who have died. In the recent cases covering the past two years it is hoped that as the result of early recognition and prompt radical surgery survivals of five to ten years will be the rule rather than the exception.

Plastic & Reconstructive Surgery, Baltimore

2: 517-644 (Nov.) 1947 Partial Index

Restoration of Nose, Lip and Maxilla by Surgery and Prosthesis. V. H. Kazanjian.—p. 531.
*Treatment of Facial Paralysis by Tantalum Wire Suspension: Preliminary Report. L. W. Schultz and E. F. Fowler.—p. 538.
Free Skin Graft—Immobilization with Plaster. L. Zeno.—p. 549.
Surgical Treatment of Pressure Sores. S. Gordon.—p. 557.
Use of Neck Tubed Pedicles in Reconstruction of Defects of Face. W. B. Macomber and W. T. Berkeley.—p. 585.

Tantalum Wire Suspension in Facial Paralysis.—Schultz and Fowler say that Schuessler has substituted tantalum wire and thin sheet tantalum saddles in place of fascia lata as the suspensory material. Advantages claimed for this method induced the authors to utilize Schuessler's method in 2 cases. They noticed a tendency of the saddles to cut through the muscle bundles. One other disability produced by a complete facial paralysis is the inclination toward ballooning out of the paralyzed cheek in the enunciation of certain syllables. Futhermore, patients with facial paralysis who must wear dental plates have difficulty in maintaining their denture in position, since the action of the musculature of the unparalyzed cheek acts to force the denture toward the paralyzed side and loosen its contact with the alveolar ridge. The use of tantalum gauze in the repair of hernial defects suggested to the authors a means of overcoming both the cutting effect of the saddles and the flaccidity of paralyzed cheek muscles. They believe that if moderately large segments of tantalum gauze are implanted in the facial tissues the surrounding fibrous bands of tissue growing through the mesh will allow a more equitable distribution of the pull placed on them by a tantalum wire suspension than would a similar pull placed on the small amount of tissue enclosed by a tantalum saddle. Such an implanted gauze of tantalum wire will, if made sufficiently large and accurately placed, also lend support to the atrophic cheek and will aid in prevention of the ballooning out effect and the unwelcome mobility of the dentures. Case reports illustrate experiences both with Schuessler's method and with the modification developed by the authors. They admit that the suspension of paralyzed muscles cannot produce a result comparable to that produced by a repair of the facial nerve, which adequately reinnervates the paralyzed facial musculature.

Psychoanalytic Quarterly, Albany, N. Y.

16:459-618 (Oct.) 1947

Psychodynamics of Masochism. B. Berliner.—p. 459.
Some Observations on a Form of Projection. I. J. Saul.—p. 472.
Basic Mental Concepts: Their Clinical and Theoretical Value. E. Glover.—p. 482.
Fallacious Use of Quantitative Concepts in Dynamic Psychology. L. S. Kubie.—p. 507.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Urology, London

19:197-260 (Dec.) 1947. Partial Index

Aseptic Prostatectomy. F. E. Stock. -p. 206.
Chronic Pyelonephritis. J. H. Carver. -p. 223.
Case of Renal Carbuncle Treated by Penicillin. W. R. S. Hutchinson and J. V. S. A. Davies. -p. 229.

Indian Medical Gazette, Calcutta

82:443-508 (Aug.) 1947. Partial Index

Hypoproteinemia Due to Utilization of Plasma Protein for Erythropoiesis. C. B. Das Gupta and J. B. Chatterjee. -p. 445.
Further Observations on Plague. A. T. W. Simeons and K. D. Chhatre. -p. 447.
Blackwater Fever. A. K. Nandi. -p. 451.
*Death From Sternal Puncture. P. N. Bardhan. -p. 459.
Suprapubic Prostatectomy with Special Reference to Penicillin Treatment. A. D. Bhandari. -p. 469.

Death From Sternal Puncture.—Bardhan presents histories of 2 patients in whom death occurred after sternal puncture. The guard on the puncture needle, which had been at 8 and 11 mm., respectively, in these 2 patients, had not slipped. In both cases the needle had punctured the posterior plate of the sternum only to a minute degree. However, the resulting laceration in the right ventricle was nearly an inch (2.5 cm.) long in each case. Subsequent studies on cadavers indicated that with the force of the jerky movements associated with sternal puncture, the sternum could be pressed down for nearly an inch and the soft tissues could be reduced in depth up to 4 mm. If the anterior mediastinum, which is, after all, only a potential space, is fully obliterated by the heart and there is an unsuspected increase in the range of the needle, there is nothing to prevent a traumatic rupture of the heart. There can be little doubt that the two deaths occurred in the foregoing manner. Apprehension caused holding of the breath; this in turn led to stretching of the heart and its approximation to the sternum. Jerky movements caused an unsuspected increase in the range of the needle. The needle then pierced the posterior plate of the sternum and caused a small prick in the heart. The heart having been put on maximal stretch, the prick rapidly became converted into a laceration by the rising intracardiac pressure. Hemopericardium followed, leading to mechanical arrest of the heart and to death.

Lancet, London

2:933-968 (Dec. 27) 1947

Visceral Pain. H. Cohen. -p. 933.
Comprehensive Student-Health Service. A. H. Hochlin. -p. 935.
Compulsory Physical Education for University Students. R. H. Bolton. -p. 938.
Health Examinations of Students: Pilot Survey in Oxford. R. V. Pownall. -p. 939.
*Familial Idiopathic Methemoglobinemia: 5 Cases in One Family. Q. H. Gibson and D. C. Harrison. -p. 941.
Rh Factor and Hemolytic Disease of Newborn in Jerusalem Jews. J. Gurevitch, A. Brzezinski and Z. Polishuk. -p. 943.
Membranous Nature of Interstitial Connective Tissue. T. D. Day. -p. 945.
Glossopharyngeal Zoster: Followed by Varicella in Two Contacts. F. J. Wright. -p. 946.

Familial Idiopathic Methemoglobinemia.—Gibson and Harrison present observations on a family with idiopathic methemoglobinemia. The condition was discovered in 1 member of this family when he attended the outpatient department of a hospital for a minor injury. He was referred to the authors because of his cyanosis, and it was found that his blood contained a considerable amount of methemoglobin. Under treatment with ascorbic acid the methemoglobin content of the blood decreased, but the patient was not concerned about his cyanotic color and did not continue treatment. Several years later his identical twin brother attended hospital for an injury. He too was cyanotic, and examination revealed methemoglobin in the blood. When he said that several other members of his family were abnormal in color, 8 of the 9 siblings were examined and 5 proved to have methemoglobinemia. The father's blood was normal; the mother, who was distantly related to the father, had died at the age of 48 but had never been cyanosed. The blood methemoglobin of patients with methemoglobinemia can be kept at a low level with daily doses of ascorbic acid, and cyanosis is then hardly noticeable. The action of a single dose of methylene blue, even when taken by mouth, is much more rapid and complete. It seems preferable, however to recommend continuous treatment with ascorbic acid, a natural food constituent, rather than with methylene blue, which might have an unsuspected toxic action after prolonged dosage. It may be desirable to supplement the action of ascorbic acid with an occasional dose of 0.3 Gm. of methylene blue by mouth, particularly if the cyanosis shows signs of returning as the result of temporary failure to keep up the intake of ascorbic acid. The authors believe that the abnormal amount of methemoglobin is due not to any defect of the bone marrow but to a disturbance in the equilibrium between hemoglobin and methemoglobin, which in turn is probably due to a deficiency in enzymes. Erythrocytes of patients with idiopathic methemoglobinemia have been observed to be deficient in a coenzyme factor.

Medical Journal of Australia, Sydney

2:677-708 (Dec. 6) 1947

Silver Spoons and Golden Genes. A. Newton. -p. 677.
*Investigation of Benzene and Toluene Poisoning in Royal Australian Air Force Workshops. Mildred Hutchings, Sheila Drescher, F. B. McGovern and F. A. Coombs. -p. 681.

Benzene and Toluene Poisoning in Air Force Workshops.—Hutchings and her associates during 1944 undertook investigation of the effects of contact with aromatic naphthas on persons working in air force workshops. This large scale investigation was precipitated by the death of an airman from agranulocytosis and thrombocytopenia. The patient had been employed for two months, for one and a half hours per day, cleaning engine parts with kerosene and gasoline after the parts had been removed from a cleaning fluid of high benzene content; zinc chromate spraying was also carried on in the hangar, and the fumes were rather heavy during spraying. The postmortem examination revealed aplasia of the leukocyte and platelet elements; the red cells appeared to be affected to a lesser degree. From this and the patient's history of contact with benzene, it was concluded that the condition was due to benzene poisoning and that other personnel in contact with the agents should be investigated. An analysis of the fluids containing aromatic hydrocarbons included an engine cleaning fluid, various paints and thinners, and a rubber solution. The aromatic hydrocarbon content varied from 16 to 56 per cent. An estimation of the aromatic hydrocarbon content of the atmosphere showed variations between 0 and 1,400 parts per million. The higher concentration existed only for short periods, but for the major portion of the time the concentrations were 10 to 35 parts per million. On the basis of their obser-

vations, the authors conclude that there is no need for routine blood examinations of men working in engine-cleaning and painting shops, provided that exposure is minimized. The authors outline the steps taken to provide good working conditions. New processes involving the use of different solvents are constantly introduced, and there is an urgent need for close cooperation between the technical services and the medical services, in order that adequate precautionary measures be taken.

Arch. del Inst. de Cardiol. de México, Mexico, D. F.

17: 761-870 (Dec. 31) 1947. Partial Index

*Study of 1,160 Cases of Rheumatic Valvular Endocarditis. C. Cortés and H. Villarreal. -p. 775.

Rheumatic Valvular Endocarditis.—Clinical records of 1,160 patients with rheumatic valvular endocarditis were studied in the National Cardiologic Institute of Mexico. Records of 147 necropsies in the same institution on bodies of patients who died with the disease were also studied. In the group of 1,160 patients there were 737 females and 423 males. Race was not a predisposing factor. A history of rheumatic fever was recorded in 656 patients and of chorea in 152 patients. Rheumatic heart disease without history of rheumatic fever was recorded in 430 patients. In the majority of cases the first attack of rheumatic fever was recorded between the ages of 11 and 20 years and the appearance of chorea between the ages of 6 and 10 years. Joint pain was the predominant symptom in most cases. The clinical diagnosis of valvular involvement was mitral in 1,122 cases, aortic in 209 and tricuspid in 20. Cardiac failure occurred in 512 patients. It appeared most frequently in patients between the ages of 20 and 40 years, especially in a variable period from three to ten years after the first attack. Disturbances of cardiac rhythm were encountered in 203 patients and of conduction in 69 patients. Fibrillation coexisted with mitral stenosis in 189 patients. Rheumatic heart disease coexisted with congenital disease in 6 cases, with syphilitic heart disease in 102 cases, with bacterial endocarditis in 18 cases and with hypertensive heart disease in 42 cases. Clinical diagnosis of the following complications was made: pericarditis in 16; pleuritis, 11; pulmonary infarct, 14; peripheral embolism, 41, and renal involvement, 26. The highest death rate occurred in patients between 11 and 20 years of age. Mitral stenosis and mitral disease were encountered in the majority of necropsies which revealed these complications and also in the majority of necropsies on the bodies of 127 patients over 44 years of age. Valvular syphilitic lesions were frequently encountered in the patients over 44 years of age.

Archivos de Pediatría del Uruguay, Montevideo

18: 553-594 (Nov.) 1947. Partial Index

*Penicillin in Gonorrhea in Children: Ambulatory Treatment by Injections. A. Wiederhold and A. Blández. --p. 576.

Gonorrhea in Children.—Twenty-five children between the ages of 8 months and 12 years with gonorrhea were given penicillin therapy by mouth for six months followed by clinical and bacteriologic cure. The dose of the drug varied between 300,000 and 600,000 units. Penicillin by the mouth is rapidly eliminated in the urine, in sufficient concentration to kill gonococci. Treatment is simple, easy to administer and reliable. Patients have been observed for more than one year after recovery. None had a recurrence. Another group of 26 children between the ages of 2 and 12 years, also with gonorrhea, had intramuscular injections of penicillin in doses which varied between 100,000 and 250,000 units. Clinical and bacteriologic cure was obtained in 21. The purulent discharge and the presence of gonococci in the microscopic preparations of the secretion were maintained in the other 5. Higher doses of penicillin by the intramuscular route failed to cure the disease.

Gynaecologia, Basel

124:257-320 (Nov.) 1947. Partial Index

Sensory and Motor Innervation of Uterus. E. Held.—p. 257.
Simple and Successful Method of Formation of Artificial Vagina. F. Kovacs.—p. 290.
*Nutrition of Pregnant Woman in Relation to Malformations of Newborn. S. van Creveld.—p. 299.

Nutrition of Pregnant Women and Malformations in the Newborn.—Van Creveld reviews experimental investigations carried out in recent years which demonstrated the great importance of the diet during pregnancy in connection with the occurrence of deformities in the progeny. A relationship between an unsuitable diet in pregnant women and the occurrence of congenital deformities in the infants must be considered. He cites the case of a baby whose weight at birth was 2,600 Gm. and who had a partial cleft palate, together with micrognathia and partial syntarsalia of the second and third toe on both feet. The families of the father and mother were free from malformations, and parents as well as an older child were normal. During the pregnancy the maternal nutrition had been deficient in protein with hardly any fruit and little butter and fat. Observations on a group of 216 stillborn babies and infants who died within a few days after birth are suggestive. The majority of infants with evident congenital malformations and all premature babies were born of mothers whose nutrition during pregnancy had been extremely inadequate. In comparison, 91 per cent of the mothers whose babies were well at birth had had either a good or a fairly good diet during pregnancy. It has been demonstrated that if the mother contracts certain virus diseases, such as rubella, during the early months of gestation fetal deformities are likely to result. The author believes that the damaging effects of poor nutrition are exerted on the fetus chiefly during the latter part of gestation.

Journal d' Urologie, Paris

53:401-528 (Nos. 10 & 11) 1946-1947

*Amino Tumors of Bladder (Called Aniline Tumors): Seventeen Cases Observed in France. J. L. Billiard-Duchesne. -p. 401.
Medicosurgical Treatment of Cancer of Prostate: Subcapsular Orchidectomy and Hormone Therapy. A. Cassuto. -p. 423.
Rupture of Corpus Cavernosum (Improperly Designated as Rupture of Penis). A. Puigvert and J. Iscies. -p. 431.

Amino or Aniline Tumors of Bladder.—Billiard-Duchesne states that physicians in industrial practice for years have observed the frequent occurrence of hematuria among employees of plants where dyestuffs are produced. Tumors of the bladder, which are often found, are now recognized as of occupational origin and are designated as aniline tumors. "Aniline tumor of the bladder" is not quite correct, since aniline itself does not produce these tumors. Only certain compounds of the aromatic amines are regarded today as carcinogenic, namely, benzidine, alpha-naphthylamine, beta-naphthylamine, 4'-amino-2,3' azotoluene and 2-acetylaminofluorene. Data on the 17 cases under consideration reveal that ages of the patients vary between 39 and 74 years, the average being 53 years. Since this is the age at which tumors develop spontaneously, age may play a secondary role. In only 2 to 5 per cent of those with prolonged exposure do tumors develop; this suggests that some personal predisposing factor may occur. Single as well as multiple tumors occur; they may appear in any part of the bladder but especially in the lower half. Of 7 histologically examined tumors, 6 were cancerous and 1 was noncancerous. Differential diagnosis of an occupational and a spontaneous

tumor must be based chiefly on a history of exposure and the occurence of such tumors in similarly exposed workers. Preventive measures suggested by the author include avoidance of more than five years of occupational exposure to substances like benzidine and alpha-naphthylamines and beta-naphthylamines; thorough preemployment examination and inquiry with regard to earlier employment in plants producing dyestuffs; the use of closed processes wherever possible; good ventilation; frequent washing of hands by the workers and a daily shower; periodic examination of blood and urine, and systematic cystoscopic examination of workers who have been exposed for five years.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

91:3585-3664 (Dec. 13) 1947. Partial Index

Carcinoma of Corpus Uteri. M. A. van Bouwdijk Bastiaanse. -p. 3588.
Infarct of Uterus. A. J. M. Holmer. -p. 3590.
*Complications After Salpingography. P. S. ten Berge-p 3594.
Polymorphism of Erythroblastosis Fetalis. G. J. Kloosterman. -p. 3610.
Importance of Rupture of Membranes at Onset of Labor Pains. E. Tonkes. -p. 3616.
Reinfusion of Own Blood in Abdominal Hemorrhages, Particularly in Extrauterine Pregnancy. P. J. Hoedemaker. -p. 3619.
Stomach Cramps in Impending Eclampsia. H. Heyster. -p. 3622.

Complications After Salpingography.—Ten Berge believes that gynecologists and radiologists give too little attention to the dangers of salpingography. Histories of 4 patients are presented in whom serious complications resulted from salpingography, with one death. The author recommends pertubation in place of salpingography. Danger of air embolism in pertubation is obviated if carbon dioxide is used instead of air. Although pertubation involves less danger than does salpingography, it too may cause a reaction in an infected focus, as illustrated by the author's fifth case. However, the reaction takes a milder course than does that elicited by salpingography.

Praxis, Bern

37:1-20 (Jan. 8) 1948

*Refrigeration in Treatment of Arterial Obliterations of the Extremities. G. Bickel and J. Fabre. -p. 1.
Problems of Fight Against Cancer. A. Zappinger. -p. 6.
Some Actual Problems of Physiotherapy, Hydrology and Medical Climatology. K. M. Walthard. -p. 10.

Refrigeration Treatment.—Bickel and Fabre treated 4 patients, 3 women between the ages of 72 and 80 and 1 man aged 80, with gangrene of the lower extremities from obliteration of the arteries, by refrigeration. Amputation was postponed because of severe cardiopathy, advanced cachexia or refusal of surgery. The extremities involved were covered with a stocking of fine wool and then wrapped with ice bags up to 10 cm. above the ischemic zone. The ice was renewed every four hours. Refrigeration was discontinued every day for three hours. The extremity treated in this manner is cooled but not frozen. The nutritive requirements of the cells are reduced by a maximum, the formation of toxins responsible for the occurrence of shock is diminished, the exudative processes are limited, proliferation of pathogenic microbes is inhibited and a pronounced anesthetic effect is produced. Pain subsided within two hours after the initiation of the treatment. There was pronounced improvement in the local condition; in 1 case the ischemic zone was reduced by 6 cm.; in another case mummification of the previously moist and septic gangrene occurred and edema and suppuration subsided. The general condition improved rapidly, temperature was restored to normal and appetite increased. Amputation could be performed after two weeks of refrigeration treatment.

Presse Medicale, Paris

56:1-12 (Jan. 3) 1948

Metabolism of Lipids in Ieterohemorrhagic Spirochetosis. P. Nicaud. -p. 1.
Cervicoabdominal Tunnelization (Subcutaneous Anastomosis) in Carcinoma of Esophagus. C. Olivier. -p. 2.
*Mortality From Diphtheria in Vaccinated and Nonvaccinated Persons. N. Blanco-Otero. -p. 3.
Technic of Intratibial Injection in Suckling Infants. R. Couder. -p. 4.

Mortality From Diphtheria.—According to Blanco Otero, vaccination with diphtheria antitoxin was initiated in Spain in 1940 and was practiced on a large scale. It became compulsory in 1943. With the first year of vaccination the mortality rate from diphtheria decreased by 50 per cent; the following year it decreased by 75 per cent. Within three years the mortality in the province of Soria dropped from 40 per hundred thousand inhabitants to 3; in the province of Segovia the mortality rate dropped from 29 before the prophylactic campaign to zero. A survey of the mortality in twenty-nine provinces revealed that of 702 persons who died from diphtheria, 659 had not received any vaccine, while 43 had been given a total or partial dose of vaccine. There was only 1 case of diphtheria and no fatality among 2,000 children aged less than 3 years who were vaccinated by the author in the district of Congreso (Madrid), and this during an epidemic and in children who lived under poor hygienic conditions. The mortality continued to decrease up to 1946, when it was one-fifteenth that in 1939, decreasing from 15.7 in 1939 to 0.9 in 1946.

Revue Médicale de Liege

2:629-652 (Dec. 15) 1947

*Clinical Trial with Di-Insulin. L. Brull and others. -p. 631.
Facts and Considerations with Regard to Diagnosis of Hypovitaminosis C. G. Barac. -p. 640.

Clinical Trial of Di-Insulin.—Brull and his co-workers treated 42 patients between the ages of 22 and 77 who had diabetes mellitus with di-insulin. 'Di-insulin,' a Danish preparation, is a mixture of equal amounts of ordinary insulin and of Hallas-Møller's "iso-insulin" (phenylureidoinsulin); the two insulins are miscible without affecting each other; i. e., the protracted action of the "iso-insulin" does not protract the action of the ordinary insulin. A wide V form of the twenty-four hour blood sugar curve is obtained, with two hypoglycemic notches, the hypoglycemic maximum being reached seven to eight hours after the injection. Results demonstrated that "di-insulin" may be used with advantage in all forms of diabetes mellitus by giving two injections of 30 units, 60 units daily, to patients with moderately severe or severe diabetes and by one injection of 30 units daily in mild diabetes. Doses of 50 units administered in one injection were well tolerated and did not cause hypoglycemia. As compared to ordinary insulin or to protamine zinc insulin, "di-insulin" has the following advantages: reduction of the total dose administered, reduction in number of injections, better control of the glycemia and particularly of the glycosuria. Patients with severe diabetes mellitus requiring massive doses of ordinary insulin or of insulin with protracted action are benefited by changing to "di-insulin."

Book Notices

Afecciones vasculares quirurgicas del encefalo. Por el Dr. Alfonso Asenjo F.R.S., F.A.C.S., director del Instituto central de neurocirugia, Chile, y el Dr. Enrique Ulberall, Consultor neurologo de la Clinica médica del Hospital San Borja y de la Sección B de medicina del Hospital del Salvador de Santiago, Chile. Paper. Pp. 308, with illustrations. Central de Publicaciones, Casilla 9J, Santiago, Chile, 1945.

This monograph is based on a review of the literature and 32 cases studied by the authors, some of which were observed in Europe. The iconography, however, is new. The book is well illustrated but some of the roentgen photographs have been too much reduced so that the lesion is difficult to see. The authors use their own classification of these lesions, distinguishing the angiomatoses from the tumors. The congenital malformations are divided into (*a*) cavernomas, (*b*) telangiectases, (*c*) Sturge-Weber-Dimitri disease, (*d*) angiomas, venous and arterial and (*e*) arteriovenous aneurysms. The acquired angioses are traumatic arteriovenous fistulas and sacciform aneurysms. The tumors discussed are the hemangioblastomas of Lindau, angiogliomas and angioblastic meningiomas. The discussions of symptomatology, pathology, diagnosis and treatment follow classic lines, except that the authors believe pure arterial angiomas to be very rare. They use arteriography in the diagnosis, and the procedures outlined for treatment are reasonable and conservative. This monograph is an interesting and reliable guide for Spanish-speaking physicians.

Do You Have Body Control? Edited by Mrs. Helen J. Campbell. Prepared for Punahou School Girls. Physical Education Department, Honolulu, T. H. Exercises Designed by Miss Ruth Aust. Paper. Price, 50 cents. Chart; no pagination, with illustrations by Mrs. Bertha Lowrie, Miss Ruth Aust, 358 Young Hotel Building, Honolulu 9, T. H., 1945.

This pamphlet offers suggestions and describes exercise designed to bring about "body control," which is defined as the efficient use of the body in any movement. The brochure can be unfolded to form a large wall chart portraying a series of twelve exercises in black and white. Muscles coming into greatest use in each of the stunts are differentiated in the illustrations. Directions accompanying the exercises are clear and concise, and the illustrations are attractive. Some of the exercises are relatively strenuous and would require adaptation for persons long out of training or who have not practiced vigorous exercises regularly. Among the maxims found on the reverse side of the chart are suggestions relating to choice of exercises, learning to relax, improving posture and the value of physical recreation! In the school situation with adequate medical and educational supervision these charts may have real value. Indiscriminate use by the layman might on the other hand involve certain hazards, since directions include the prescription of local exercises for specific conditions. Precautions need to be set up by which all persons undertaking such an exercise routine will be ascertained through medical examination to be organically sound. Additional emphasis on the factors of suitable work, adequate nutrition, rest, relaxation, the use of preventive and therapeutic medical services and the avoidance of excesses might well be given.

The Twentieth Century Fund, Annual Report 1946. Paper. Pp. 47. The Twentieth Century Fund, 330 W. 42d St., New York 18, 1947.

The Twentieth Century Fund produces each year a relatively few publications. Recently they published the survey volume, "America's Needs and Resources," and the "Report" of the Fund's Foreign Economic Committee. The report indicates that the Fund spends half its current income on research—that is to say, on the execution of research projects through to publication—and 40 per cent on dissemination of information. Ten per cent of its income goes for overhead. The work in developing methods of public information may become the most significant contribution of the fund as a whole. Experiments have been made with motion picture and radio presentation of the results of the fund's research. Cooperation has been fostered with the chamber of commerce, the Y. M. C. A., the federal council of churches and the advertising council.

Pharmaco-Therapeutic Notebook. By H. W. Tomski. With a foreword by Hugh A. Dunlop, M.D., M.Sc., F.R.C.P. Cloth. Price, $4.50. Pp. 250. William Wood & Co., Mt. Royal & Guilford Aves., Baltimore 2, 1947.

This book was prepared to furnish pharmacists "essential notes on the various aspects of pharmaceutical practice." Designed for the British pharmacist, this book fails to carry out its purpose and is even less suitable for American pharmacists. The book presents short descriptive statements regarding a number of drugs arranged in groups according to the predominating pharmacologic action. However, the statements offer little or no pharmacologic information and deal chiefly with the clinical use of the agents. The selection of agents to be discussed is often unfortunate, and many of the recommendations are uncritical. For instance, among the recommended antimalarials are found Fowler's solution with iron and quinine (Bacelli's mixture) and sodium cacodylate. Mercury preparations are recommended for syphilis. A weird mixture of lithium and sodium hippurates is recommended for use in conjunction with various nitrites as a "hypotensive." The use of Latin titles cannot be criticized, since their use is customary in Great Britain, but many of the names applied to drugs common in this country will be confusing to the American pharmacist.

Differentialdiagnose der Lungenröntgenbilder; Besonders Berucksichtigung derjenigen Erkrankungen, die mit der Lungentuberkulose verwechselt werden können. Von Dr. Med. Rudolf Zoerleder. Mit einem Vorwort von Pd. Dr. Med. J. Horin und Dr. Med. H. Stöcklin. Second edition. Cloth. Price, 28 Swiss francs. Pp. 296, with 93 Illustrations. Hans Huber, Marktgasse 9, Bern 16, 1947.

This well prepared monograph considers most of the lesions that are seen by the roentgen examination. The author has arranged his material in a rather interesting form, considering lesions seen in the lung and mediastinum. The author discusses the diagnostic criteria clinically and roentgenologically and considers the conditions from which the various lesions should be differentiated. The book contains two hundred and ninety-six pages of text, reference and index, and there are ninety-three illustrations with drawings where it was necessary to emphasize shadows seen in the roentgenograms. The form of the book is not new, as a number of other authors have attacked the same problem in a similar way. Nevertheless this book is an addition to the roentgenologic literature and should bring help to those who can read German. The publishers have furnished a satisfactory paper, the print is readable and the illustrations are excellent. However, it should be stated that the illustrations are positive instead of negative.

Fracturas del extremo inferior del radio. Por el Dr. José A. H. Bulfaro. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas. Paper. Pp. 243, with 144 illustrations. Buenos Aires, 1946.

This is a Ph.D. thesis covering a circumscribed field, but the subject is handled thoroughly and scientifically. The monograph considers both para-articular and juxta-articular fractures of the radius as well as associated lesions. They are discussed from all angles, etiology, symptomatology, diagnosis and treatment, and this is prefaced by a short but entirely adequate review of the anatomy and kinesiology related to the subject, not omitting the radiologic aspect for which some valuable diagnostic hints are offered. The roentgenograms are sharp and clear, and their reading is considerably assisted by sketches placed beside them. The book is well written and clear and is amply documented by case reports. The classification is practical, the treatment simple and not unnecessarily complicated. The author's experience is well evidenced by many cases. Some new technical items are mentioned, such as the fixation clamp used for traction and mechanical devices for traction and spreading of the fingers with a new articulative factor for the thumb, which are simple and rather practical. The book is well worth reading and is a definite contribution to this subject.

The Selected Writings of Benjamin Rush. Edited by Dagobert D. Runes. Price $5. 433 Pages. The Philosophical Library, 15 East 40th Street, New York, 1947.

Mr. Runes deserves credit for assembling the "cream" of Rush's writings. More ought to be said and written about this truly great American, for there are many patriotic Americans who do not know even that he was a signer with Franklin of the Declaration of Independence!

Rush was born the day before Christmas (Dec. 24, 1745) on his father's farm just north of Philadelphia and was fortunate in having a highly educated and inspiring uncle, the Rev. Samuel Finley, who was headmaster in the academy and later took his nephew in as a student there. The boy must have been brilliant, for he was graduated from Princeton before the age of 15 and then spent six years studying under Dr. Redman as preceptor, as was the custom in those days, after which he went to Edinburgh and received his M.D. in 1768, aged 23. Then came a trip across the Channel to France, but he seems not to have cared much for the medical science he found there. He returned to Philadelphia, took an instructorship in chemistry in the College of Philadelphia, the first medical school in America, and eventually received an appointment as professor of the institutes and practices of medicine when the College became a university in 1791. Rush mingled with men in all stations of life and acquired much information, which he reduced to facts in the crucible of his fine mind. His interests and energies covered an amazing field and would be noteworthy even were he living today. Some of the titles to his papers have to do with slave keeping, to which he was opposed, a plan to make the United States a universal peacemaker, on helping the Africans, the defects of the confederation (not all the signers of the Declaration thought it sacrosanct), securities for liberty, capital punishment (to which he was opposed) and the essentials of good government. He had thought widely and deeply on the education which is best suited to a republican form of government and conceived a plan for a federal university. By nature Rush was sanely religious and recommended the Bible as a sort of textbook in the schools of his day. Natural and medical science were to him so closely allied that he lectured on animal life as a basis for the study of human physiology. He wrote on the different species of mania and phobia and on the "progress of medicine" (1801). Physicians have vices and virtues, which he carefully catalogs and then concludes that the virtues exceed the vices by far in the daily balance. There is a lecture delivered to medical students on the "duties of physicians," which, of course, were no different then than now. Among the titles listed in this book are an inquiry into the ways of the American Indian and his "medicine," concerning the climate of Pennsylvania, an account of bilious fever, the cause and cure of cholera infantum, common salt as a cure for hemoptysis, thoughts on "pulmonary consumption," arsenic in the cure of external cancers, on tetanus, medicine in the Revolutionary war, a new method for inoculating against smallpox, the noncontagiousness of yellow fever, the influence of alcohol and tobacco on human health and morals, the sugar maple tree in the United States and medical inquiries and observations on diseases of the mind.

Orthopedic Surgery for Nurses Including Nursing Care. By Philip Lewis, M.D., F.A.C.S., Professor of Bone and Joint Surgery, Northwestern University Medical School, Chicago. Fourth edition. Cloth. Price, $3.75. Pp. 563, with 255 illustrations. W. B. Saunders Co., West Washington Square, Philadelphia 5, 1947.

In this edition there have been certain important revisions. Information on poliomyelitis is brought up to date, and the section on preventive and postoperative measures is added. There is also an addition to some of the technical part such as strapping. The book should be judged from the point of view of furnishing information on orthopedics for nurses rather than as a book on strictly nursing technic. In this respect the book is admirably suited for its purpose. The information is thorough and detailed enough to be of real practical use without going too much into theoretic considerations. The description of operations and their purposes is clear, concise and adequate for the instruction of nurses. This book is a leader in its line and should be a valuable and indispensable addition to any library for nurses.

Precis de Dermatologie. Par J. Darier, A. Civatte et A. Tzanck. Fifth edition by A. Civatte. Cloth. Price, 1700 francs. Pp. 1352, with 300 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1947.

A. Civatte has followed closely the plan of the previous editions by Darier and has changed the clinical descriptions in only slight degree, although he has discussed the more recent developments in dermatology with respect to etiology, pathogenesis and physiology. The present textbook retains the usual division of previous editions into two main categories, morphologic and nosologic, often requiring the reader to consult both sections. The clinical descriptions, however, remain outstanding in their clear and concise presentation of the essential data on the various dermatoses, and the book is unsurpassed as a reference in this respect. The author states that he has adhered to Darier's desire to limit the text to the scope of a manual, and consequently relatively few of the more recently described dermatoses are included in this new edition. The text can be recommended only for those who wish to find a maximum amount of information regarding the chief clinical characteristics of the well established dermatoses. An appendix thirty-eight pages long deals with treatment, covering general therapeutic considerations and offers a number of prescriptions to meet special indications.

The Rehabilitation of Speech: A Textbook of Diagnostic and Corrective Procedures Based upon a Critical Study of Speech Disorders. Book One: The Pathology of Speech and the Rationale of Its Rehabilitation. By Robert West, Professor of Speech Pathology, University of Wisconsin, Madison. Book Two: Remedial Principles. By Lou Kennedy, Associate Professor of Speech, Louisiana State University, and Anna Carr, Clinical Adviser in Speech, State Teachers College, Milwaukee. With a Chapter by Ollie L. Backus, Assistant Professor of Speech, University of Michigan, Ann Arbor. Book Three: Case Histories. Second edition. Cloth. Price, $5. Pp. 650, with 39 illustrations. Harper & Brothers, 49 E. 33rd St., New York 16, 1947.

The new edition of this well known textbook reports chiefly the personal experiences and opinions of the authors. The aspect of the medical specialist in the field of speech and voice pathology is given little consideration. As a result the medical reader will not accept some of the text or some of the illustrations, for instance, figure 21. That "whispering is harmless" in some disorders of the voice has been disproved by Dr. Hogewind. Lethargic encephalitis is not identical with sleeping sickness (p. 165). Some reliable methods to test the hearing of very young children have not been mentioned. Among the dyslalias the important clinical picture of multiple interdentality has been ignored. In the chapter on stuttering group treatment is recommended, although the group treatment of any other form of neurosis has not been accepted by most psychotherapists.

In general the book is a comprehensive study and offers to the reader useful information about the most important speech and voice disorders. Helpful therapeutic procedures are described, although there are a number of others which have been proved efficient and in some special cases superior. The fact that the book is a compound work accounts for the repetition of some of the material from chapter to chapter. The glossary containing some four hundred items is an excellent feature for the reader who needs easily to find terms briefly described.

The Yearbook of Psychoanalysis. Volume 2. Managing editor: Sandor Lorand, M.D. Fabrikoid. Price, $7.50. Pp. 280. International Universities Press, 227 W. 13th St., New York 11, 1946.

This is a collection of fourteen articles, mostly from well known psychoanalysts. There is no introduction to explain this special selection. It begins with a methodical article by Hartman and Kris defending the conservative point of view in this field which only recently has begun to emancipate itself from the domination of traditional views and practices. Fenichel in an article on psychosomatic phenomena essentially accepts Alexander's distinction between conversion symptoms which have a symbolic meaning and vegetative responses to emotions often called "organ neuroses." A lucid article of French on ego analysis contributes greatly to the value of this volume. Four articles by English authors (Jones, Flugel and Glover) are included. The volume contains the translated article of Freud: "Dostoievsky and Parricide." This is a penetrating analysis of "The Brothers Karamazov" which, like Hamlet and Oedipus Rex, is an intuitive elaboration of the Oedipus complex.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

RHEUMATIC HEART: TROPICAL CLIMATE

To the Editor:—Because of the difference of opinion existing in the literature and among pediatricians and cardiologists regarding the advisability of moving a child 8 years of age with inactive minimal rheumatic mitral insufficiency to a tropical or semitropical climate, I would appreciate an authoritative opinion. If affirmative, please send information regarding the most suitable locations, preferably but not necessarily in the United States or its possessions.

Ralph C. Grosse, M.D., Memphis, Tenn.

ANSWER.—As indicated in the question, scientific data are not available on which one may base an answer acceptable to all observers. There are many features to be considered, some of which may be briefly mentioned:

1. There are known areas of high and low incidence of rheumatic fever in the United States. This is better recognized now as a result of World War II experience with rheumatic fever. The data assembled by Hedley, the Metropolitan Life Insurance Company and the war experience are in close agreement. However, rheumatic fever may occur in any part of the United States, and all surveys conducted by experienced observers indicate that there may be more rheumatic fever and/or rheumatic heart disease in low incidence areas than was previously supposed.

2. Claims of observers that specific areas offer particular advantages over other locations have not yet been substantiated by satisfactory scientific data. Once rheumatic fever is active, there exists no proof that any climate alters the severity or duration of the disease or the outcome in the given instance.

3. Exposure to epidemic factors (group A, beta hemolytic streptococcus infections) influencing the natural history of rheumatic fever vary considerably in various parts of the United States. However, rapid transportation may alter this and make it necessary for rather complete isolation even in low streptococcus infection areas. This would mean a rural life and probably poor medical supervision. Further, the possible effect on immunity from long residence in such an area is unknown. There is a strong probability that such a residence must be permanent and continuous not only for the patient but for the patient's immediate personal contacts (family).

4. The usual environment (described by Paul as microclimate) of the person recovered from rheumatic fever or the possibility of greatly improving the environment without change in climate must be considered. Much can be done, in areas where rheumatic fever is common, to decrease exposure to hemolytic streptococcus infections.

5. Experienced observers in areas where rheumatic fever is common report that two thirds of those with rheumatic fever do well although remaining in the area where the disease begins.

6. Sulfonamide prophylaxis (and perhaps eventually penicillin prophylaxis) under careful medical supervision may greatly improve the foregoing results.

7. Psychologic and economic factors vary greatly and must be considered in each instance in which advice is to be given.

8. In the great majority of instances, transportation to another climate is impractical and cannot be considered as the solution to this many-sided problem.

INDELIBLE PENCILS

To the Editor:—A woman got a fragment (about 1 by 1 by 2 mm. in size) from an indelible pencil in her left oculo-ocular (eye). After twenty-four hours it was removed, leaving a small ulcer of the conjunctiva and a purple stain about 2 cm. in diameter. Aside from irrigations and anesthetic ointment, could any other treatment have been used? One week later vision was 25/20 and the stain had been completely absorbed.

Arthur H. Dougherty M.D., Dodge City, Kans.

ANSWER.—Indelible pencils are most commonly made of an aniline dye which is exceedingly corrosive, and wounds caused by them are, as a general rule, of a serious character. Unless the pencil lead with the stained tissue is promptly removed, the aniline dye sets up an aseptic necrosis of the tissues which results in chronic inflammation with encapsulation and cyst formation. When the orbit, the eye or any of its appendages are involved, immediate treatment must be instituted by removing the fragments of the staining substance and all surrounding necrotic tissue, as well. Postoperative irrigations of 5 to 10 per cent solution of tannin are considered useful, as they form an insoluble compound with the aniline dye. Sodium chloride, boric acid and bichloride of mercury are contraindicated. References to this subject may be found in the *American Journal of Ophthalmology* (25:72 and 123 [Jan.] 1942; 27:1048 [Sept.] 1944) and in the book edited by Conrad Berens, "The Eye and Its Diseases," Philadelphia, W. B. Saunders Company, 1934, p. 499.

BRONCHIECTASIS

To the Editor: A patient has bronchiectasis diagnosed by iodized poppy seed oil 40 per cent (" lipiodol ") and bronchoscopy in 1939. Cough and expectoration have been the only feature up to December 1947, when the patient began to run a low grade fever that at times reached 102 F. Since then fever and increased expectoration have persisted. Bronchoscopic examination performed in January 1948 revealed an active infection and large amount of secretion coming from the left lingular division and saccular appearance of sacculi extending down into the bronchi of the lower lobe. Secretion was obtained for culture and vaccine. Culture revealed no tubercle bacilli but did reveal Neisseria catarrhalis, pneumococci and Streptococcus viridans. The patient has had a five day course of penicillin and sulfadiazine, e. g., 15 grains (0.97 Gm.) every four hours sulfadiazine and 200,000 units penicillin in oil and wax once daily. This caused decrease in cough and expectoration and slight decrease in temperature. All gradually recurred after treatment was discontinued. Aerosol penicillin was then tried, 100,000 units four times a day for seven days, with the same results. The infection has been diagnosed as mantl pneumonia. What is mantl pneumonia? What course of treatment do you suggest? Will streptomycin be of value?

H. D., Pa.

ANSWER.—The term mantl pneumonia is unknown, nor does it appear in the medical dictionaries of Gould, Dorland or Stedman. Several possibilities to account for it may be mentioned. It may be an obscure eponym, it may be a misprint or it may be mantle pneumonia, which to some may mean peripneumonia. Peripneumonia implies inflammation of pulmonary tissue around areas of abscess, bronchiectasis or other lesions in the lung.

Before treatment is resumed it would be wise to determine, if possible, what is going on, whether the bronchiectatic process is spreading, whether abscess has formed or neoplasm is present. According to experience, a five day course of penicillin therapy may not be sufficient in certain cases of bronchiectasis. Treatment may have to be prolonged for weeks. Even then there is no guaranty of relief. Nothing can restore the destroyed or defective bronchial tissue. Antibiotic therapy merely controls infection temporarily. Any subsequent minor infection of the respiratory tract is apt to cause recurrence of symptoms. Penicillin need not be injected with peanut oil or beeswax; results just as satisfactory are being achieved by the injection of 100,000 units of penicillin in its usual diluent every twelve hours. According to the flora cultivated from the exudate, there is little reason to expect that streptomycin will be helpful. It may be tried empirically if thorough penicillin therapy fails.

If conditions are suitable, lobectomy might be considered. Treatment with vaccine of any kind is illogical.

HOME HEATING

To the Editor:—Is it advisable to humidify homes in winter? If so, what is optimal humidity? In our locality, winter heating results in a sharp drop in the humidity of the home. I am particularly interested in its effect on the upper respiratory system. Frequently patients with respiratory problems are referred to dry hot climates like Arizona for relief. The Arizona climate is closely simulated by the hot dry air in our heated homes during the winter. Is it the contrasting effects of the hot dry atmosphere of the home and the relatively higher cold humidity out of doors that seems to render so many persons liable to frequent colds and flareup of latent sinus infections in the winter?

H. C. Goldberg, M.D., Plainfield, N. J.

ANSWER.—Dry air in the home during winter in cold climates has two possible effects in relation to respiratory infection. It has been found that certain pathogenic agents of the respiratory tract, e.g., hemolytic streptococci and influenza virus survive much longer in dry environments than in moist ones. (Robertson, O. H., and others: A Study of the Nature and Control of Air-Borne Infection in Army Camps, *J.A.M.A.* 126:993, 1944; Loosli, C. G., Lemon, H. M.; Robertson, O. H., and Appel: Experimental Air-Borne Infection. I. Influence of Humidity on Survival of Virus in Air, *Proc. Soc. Exper. Biol. & Med.* 53:205, 1943) Disease-producing streptococci have been recovered from blankets four and one-half months after being contaminated by carriers of hemolytic streptococci, when such blankets were kept in a dry atmosphere. Thus in a household respiratory pathogens dispersed into the atmosphere accumulate on surfaces and in fabrics when the relative humidity is low. At medium relative humidities, on the other hand, the survival of both bacteria and viruses may be brief.

Concerning the effect of different degrees of relative humidity on the upper respiratory tract in relation to respiratory infection, surprisingly little information is available. A. W. Proetz (*J. Laryng. & Otol.* 49:557, 1934) has shown that drying of the nasal mucosa results in a break in the continuity of the mucus layer which not only makes possible direct contact of foreign material (e.g., infectious agents) with the cellular surface but interferes with the ciliary action which sweeps extraneous matter away from the nasal passages.

In making comparison of the hot dry air of a heated home in a northern winter climate with the hot dry atmosphere of Arizona one must take into account the important fact that one is an internal and the other an external as well as internal environmental condition. In the latter (Arizona) situation the doors and windows will be open, thus permitting free ventilation which reduces the environmental and aerial contamination with pathogens of the respiratory tract and in such climates the human reservoirs of these disease agents are much less frequent. It is possible that rapid changes of temperature and humidity such as one experiences in northern winter climates play a role in increasing susceptibility to infections of the respiratory tract, but except for the well known predisposing factor of actual chilling of the body surface under such conditions no certain information exists. However, it has been observed for a long time that sharp rises in the incidence of pneumonia tend to coincide with rapidly changing atmospheric states. (Robertson, O.H., and others: A study of the Nature and Control of Air-Borne Infection in Army Camps, *J.A.M.A.* 126:993, 1944; Loosli, C.G.; Lemon, H.M.; Robertson, O.H., and Appel, E.: Experimental Air-Borne Infection. I. Influence of Humidity on Survival of Virus in Air, *Proc. Soc. Exper. Biol. & Med.* 53:205, 1943)

BASAL METABOLIC RATE

To the Editor:—Why is the basal metabolic rate decreased in subacute nephritis when there is no edema? What is the rationale of thyroid therapy in these cases? One of the popular methods of treatment is based on keeping the kidney at rest and keeping its metabolic activity to the minimum (e.g., "the rice diet"), and rest in bed is supposedly paramount. Would not thyroid therapy conflict with this view? The patient in question has a basal metabolic rate of minus 25 to minus 36 per cent, despite 4 to 5 grains (0.26 to 0.32 Gm.) of thyroid per day. Is there any explanation for resistance to thyroid in subacute nephritis?

M.D., Montana.

ANSWER.—The basal metabolic rate is not necessarily decreased in subacute nephritis but may be lowered by rest in bed or inactivity and by undernutrition. A low basal metabolic rate may be normal for the particular individual apart from nephritis. If this is the case or if the hypometabolism is not associated with symptoms of hypothyroidism, there is no indication for thyroid therapy. Stimulation of general body metabolism by adequate doses of thyroid is certainly incompatible with the principle of rest for the kidney or any other organ. It is difficult to find a good reason for administering thyroid to patients with nephritis in the absence of true hypothyroidism, unless one wishes to treat hypercholesterolemia empirically.

The problem of resistance to thyroid medication is of general significance. It is well established that normal, or euthyroid, persons often show little response to 2 or 3 grains (0.13 or 0.19 Gm.) or even 5 or 6 grains (0.32 or 0.39 Gm.) of thyroid daily. On the other hand, the true hypothyroid or myxedematous patient is extremely sensitive to small doses, and each grain of thyroid above the daily requirement causes a proportionate rise in the basal metabolic rate and in serum precipitable iodine or thyroxin iodine, although the basal metabolic rate changes much more slowly than the serum iodine.

Many subjects with hypometabolism can tolerate several grains of thyroid daily without change in their basal metabolic rate. They also respond less to thyroxin intravenously. Their serum precipitable iodine may remain low for weeks and months during thyroid therapy. On cessation of treatment, the basal metabolic rate may fall rapidly, indicating suppression of activity of the thyroid gland by exogenous hormone. However, resistance to thyroid is relative only; on sufficient increase in dosage and duration of treatment typical effects will be obtained, including toxicity.

From the preceding facts it may be concluded that resistance to thyroid medication is probably a function of the ability of the normal thyroid to inactivate thyroid substance. At the same time, thyroid hormone production is depressed. In states of undernutrition, response of tissues to thyroid hormone may be reduced for as yet unknown reasons.

BOILING OF MILK

To the Editor:—I assume that my practice of giving a baby whole milk at the age of eight months is generally accepted. I advise the mothers to boil this milk, even though they use pasteurized milk, for three to five minutes, at least until the child is about 1½ years of age. The mothers come back and tell me that nobody else boils the milk, why should they?

Is it advisable to insist on boiling the milk for young children although the local supply of pasteurized milk is considered satisfactory from a bacteriologic standpoint?

M.D., Wisconsin.

ANSWER.—It is the general practice today to boil milk for infants under 9 months of age. After this time, it is not necessary to boil properly pasteurized milk, considered satisfactory from a bacteriologic point of view. During the prevalence of milk-borne epidemics in any community it is wiser to temporarily resume boiling the milk until the epidemic subsides.